Science Policy Study—Hearings Volume 19
POLICIES FOR BIOMEDICAL RESEARCH

HEARINGS

BEFORE THE

TASK FORCE ON SCIENCE POLICY

OF THE

COMMITTEE ON
SCIENCE AND TECHNOLOGY
HOUSE OF REPRESENTATIVES

NINETY-NINTH CONGRESS

SECOND SESSION

APRIL 22, 23, 24, 1986

[No. 158]

Printed for the use of the
Committee on Science and Technology

U.S. GOVERNMENT PRINTING OFFICE
60-628 O WASHINGTON : 1986

For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, DC 20402

H701-36

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POLICIES FOR BIOMEDICAL RESEARCH

TUESDAY, APRIL 22, 1986

House of Representatives,
Committee on Science and Technology,
Task Force on Science Policy,
Washington, DC.

The task force met, pursuant to call, at 8:30 a.m., in room 2318, Rayburn House Office Building, Hon. Don Fuqua (chairman of the task force) presiding.

Mr. Fuqua. Our Science Policy Task Force is concluding a comprehensive review of American science policy and is examining Government policy for support of basic and applied research. The extensive series of hearings scheduled as part of this study will be completed, and our report will be issued before the end of the year. Today is the first of three hearings on the topic "Policies for Biomedical Research."

Our Government supports biomedical research not only through science agencies, such as the National Institutes of Health, National Institutes of Mental Health and the National Science Foundation, but also through mission agencies, such as the Veterans' Administration, and through regulatory agencies, such as the Food and Drug Administration. These agencies also perform research in their own laboratories. In addition, biomedical research is supported by other organizations, including private institutes, foundations, and industry. The purpose of these hearings is to examine the significant contribution of all of these supporters to the U.S. science base and to review Government policies for support of research in these fields.

The hearings will focus on three issues: first, management and coordination of biomedical research programs in the Federal agencies and other organizations; second, evaluation of research benefits; and third, direction of Government policy for support of the biomedical sciences.

During these 3 days of hearings, which will conclude on April 24, we will hear from many distinguished witnesses. Some of them will represent science, mission, or regulatory agencies; others will speak as performers of research supported by agencies or as representatives of private research institutes, foundations, or industry; and still others, as advisors or independent experts.

Today's hearing is divided into three parts. We will have a little switch today because of a change of the schedule, and I want to thank our witnesses from the National Institutes of Health for making a special effort to make it here. The panel will focus on the intramural and extramural programs, as well as the program evaluation of the Institutes. It will be made up of Dr. Joseph Rall, Deputy Director for Intramural Research; our second witness will be Dr. William F. Raub, Deputy Director for Extramural Research and Training; and the last will be Dr. Jay Moskowitz, Associate Director for Program Planning and Evaluation. Gentlemen, we are very happy to have you.

Then we will get to Dr. Salvador Luria, who is a Nobel Laureate and former Director of the MIT Cancer Center, who is now Institute Professor Emeritus and has had an eminent scientific career with significant contributions to basic research and extensive experience in research program management. Then our final witness will be Dr. Howard Temin from the McArdle Laboratory for Cancer Research. Dr. Temin is our second Nobel Laureate of the day. We are very honored today. And like Dr. Luria, he has made significant contributions to basic research which to a major degree have made possible our rapid progress in molecular biology. Dr. Temin will focus on Federal research programs from the perspective of the individual investigator and university.

PANEL: NATIONAL INSTITUTES OF HEALTH

First of all, let me welcome our group from NIH, and thank you again for making this special effort to be here to accommodate a change in our committee schedule.

We will begin with you, Dr. Rall.

[A biographical sketch of Dr. Rall follows:]

Dr. J. Edward Rall

Born February 3, 1920, Naperville, Illinois. Married, two children.

Education. B.A., North Central College, 1940. M.S., Northwestern University, 1944. M.D., Northwestern University Medical School, 1945. Ph.D., University of Minnesota, 1952.

Professional history. 1941–44, Teaching Assistant, Department of Pharmacology, Northwestern University. 1942–44, Research Fellow, Northwestern University. 1944–45, Intern, Wesley Memorial Hospital, Chicago, Illinois. 1945–46, Fellow, Mayo Clinic, Rochester, Minnesota. 1946–48, Medical Corps, U.S. Army. 1948–50, Resident, Mayo Clinic, Rochester, Minnesota. 1950–55, Attending Physician, Memorial Hospital, New York. 1951–55, Associate, Sloan-Kettering Institute, New York and Assistant Professor of Medicine, Cornell University Medical College, New York. 1955–62, Chief, Clinical Endocrinology Branch, NIAMD (includes assignment 1961–62 to College de France, Paris, France and National Institute for Medical Research, London, England). 1962–83 Director, Division of Intramural Research, NIAMD (later NIADDK). 1981–82, Acting Deputy Director of Science, NIH. 1983-present, Deputy Director for Intramural Research, NIH.

Professional organizations. Sigma Xi, Honors Society (North Central College), Alpha Omega Alpha, Endocrine Society, American Society of Clinical Investigation, Fellow of the American Association for the Advancement of Science, American Thyroid Association, American Physiological Society, Peripatetic Club, Association of American Physicians, American Federation for Clinical Research, National Academy of Sciences, USA, American Academy of Arts and Sciences, USA.

Honors, awards. Van Meter Prize, 1950. Flemming Award, 1959. Outstanding Achievement Award, Mayo Clinic and University of Minnesota, 1964. DHEW Superior Service Award, 1965. Outstanding Alumnus Award for Service to Profession and Society, North Central College Alumni Association, 1966. Honorary D.Sc., North Central College, 1966. Distinguished Service Award, American Thyroid Association, 1967. DHEW Distinguished Service Award, 1968. Member, Societe de Biologie, France, 1972. Docteur *honoris causa,* Free University of Brussels, 1975. Member, Royal Academy of Medicine, Brussels; Belgium, 1978. Member, National Academy of Sciences, USA, 1980. Distinguished Executive Rank, Senior Executive Service, 1980. Robert H. Williams Distinguished Leadership Award in Endocrinology, 1983.

Member American Academy of Arts and Sciences, 1985. M.D. *honoris causa*, University of Naples, 1985.

STATEMENT OF DR. JOSEPH E. RALL, DEPUTY DIRECTOR FOR INTRAMURAL RESEARCH, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, BETHESDA, MD

Dr. RALL. I am Joseph Rall, Deputy Director for Intramural Research. I am delighted to have this opportunity to testify before the Science Policy Task Force about policy for biomedical research and, in particular, how this relates to the Intramural Program of the NIH.

First, the mission of the NIH is to improve the health of the American people through research. In general, we believe that this requires us to study the most fundamental questions of biology and chemistry underlying disease, as well as to study diseases in applied diagnostic and treatment programs. NIH is a research agency. We are not a medical-care-providing agency. Although we study diseases directly, both intramurally and extramurally, for many years we have understood that our knowledge of the biological processes is so incomplete that we have to mount a major effort to learn more about how living organisms, particularly human beings, are constructed, and how they function. We really have a pitifully small amount of knowledge about the complexities of how organisms govern their metabolism, how they reproduce, et cetera, and some 90 percent of what we do know has actually been learned in the last few decades. It seems to me, biological research is the most exciting thing you can do, and I don't quite understand why all young people don't go into it.

Let me say something about the management of the Intramural Research Program. I count some 35 questions in your statement of purpose, and I will try and answer some of them as I go along.

First, how is intramural NIH managed?

All of the Institutes have an Intramural Research Program except the Institute of General Medical Sciences. Each of these programs is headed by a scientific director, and this person has overall line authority and responsibility for that particular Institute's intramural program. Nonetheless, we try to orchestrate the overall policy and guidelines in the Office of the Director of NIH. As Deputy Director for Intramural Research, I serve as Chairman of the Board of Scientific Directors, which meets every 2 weeks to discuss all scientific promotions, to discuss general policies of the intramural effort, and to discuss the external reviews, which each Institute has two or three times a year, and which I will talk about in a moment. In this way, we try to make sure that the intramural programs of the different Institutes have comparable standards and are given some sort of general oversight and guidance by the Director's Office.

The research staff, itself, comprises about 3,500 physicians, dentists, veterinarians on the campus at NIH, and we operate a 500-bed research hospital. The hospital is devoted exclusively to clinical investigation, and we provide the patient care necessary for good clinical investigation.

What is the mix of basic and applied research intramurally? Although it is not easy to define a number exactly, I would suspect it is of the order of 50 percent basic, 50 percent applied.

Who sets priorities for research intramurally at NIH? The final allocation of resources results from a very complex interplay of many factors. The NIH must accommodate scientific opportunity. Some diseases are ripe for study because we have the methods and the techniques available to approach them more or less directly; and some diseases must be studied because of their public health importance.

Legislation is particularly important, whether it be mandates, particular changes in funding, specific directions, and so forth. Some examples of legislation that set priorities include the National Cancer Act back almost 15 years ago, and more recently, increased appropriations for research into AIDS and Alzheimer's disease.

I think we understand and appreciate quite clearly that the public who pays for the research should, in a certain sense, call the tune, and in our society it is Congress who interprets the public's perception of what should be done and then directs us to do it. We feel that this is an appropriate way for the process to work. We do, however, feel that the details of exactly how to go about attacking any particular research should largely be determined by the scientists who actually do the work. A scientist who spends his life involved in some particular area of research is more likely to identify the most promising research leads, and map sometimes apparently circuitous routes required to answer important medical questions.

I quote from the Task Force on Science Policy statement, "strong central direction from the Nation's Capital may be applicable in procurement policy but may be counterproductive if applied to the Government's science program." We heartily agree with this statement.

The problem with research is that we are always trying to find the unknown, and, in general, we are most successful when we find something we didn't expect to find at all. If we had clearcut leads to pursue in every case, it would be much simpler. But by and large, when you are exploring terra incognita and there is no map—and that is basically where we are in biomedical research—all sorts of curious methods have to be tried to inch our way into the unknown.

There are so many fundamental questions that we really don't have answers to, although we now have reasonably good techniques to apply to them. The immune system, for example, is incredibly complex, and we are beginning to unravel some aspects of it. We have been trying to explore the mechanisms involved in aging, which is an extraordinarily complicated and curious phenomena. What controls the level of blood pressure? Innumerable hormones and a variety of other factors are involved, and we are gradually unraveling them. What controls the synthesis and metabolism of fat? What controls its deposition in arteries where it can cause us trouble? We are beginning to understand some of these processes. We are also beginning to understand the reproductive process, a vastly complicated interplay of multiple hormones.

I would like to say something about the infrastructure of the NIH. We have, as you well know, a campus at Bethesda of about 318 acres. Our National Institute on Aging also has extensive laboratories in Baltimore; the National Institute of Environmental Health in Chapel Hill, NC; and a large branch of the Institute of Allergy and Infectious Disease is located in Hamilton, MT, the Rocky Mountain Laboratory. Some 1,400 acres require the usual upkeep: janitors, police, managers.

Recently we have run into a particular problem with our laboratory buildings on the campus at NIH, which were built in the late thirties and early forties and are, basically, hopelessly out of date. We have started a program of round-robin renovation of these buildings. We have emptied and renovated one building and we are preparing to move into it in 2 weeks. When that move is completed, we will then refurbish the building that has been emptied. This process will probably take another 10 years, but we hope to get laboratory buildings that are reasonable and safe as a result of this phased modernization program.

A few other aspects about the NIH. It is a huge organization and its size means that we have an expert in almost any area you can think of. We also can afford a variety of expensive instrumentation, and we have tried to organize this so that we don't have duplication of facilities. Dating back more than a quarter of a century ago, when nuclear magnetic resonance was the exclusive province of the chemist, one of the Institutes set up a rather large laboratory of nuclear magnetic resonance where all the scientists at NIH utilized those instruments. Now it has turned out to be an extraordinarily useful clinical tool, and we are in the process of constructing a small building to house both magnetic resonance imaging for patients and experimental magnetic resonance imaging in which all the Institutes collaborate. Positron emission tomography requires expensive instrumentation both for the detectors and for the cyclotrons required to produce very short-lived isotopes—some of them have half-lives of minutes, so they can't easily be produced at a distance. This is all managed centrally and all the Institutes collaborate. We think it is important for large and expensive instruments to have some central management and coordination, and we manage that reasonably well.

Procurement is always a problem because science has changed somewhat. You no longer can go to a stockroom and automatically find the chemicals you need. Frequently, you have to order chemicals or reagents or isotopes almost every day, and, fortunately, we have a Division of Computer Research and Technology which has created some computerized-ordering and bill-paying systems, which have worked reasonably well.

A large part of the infrastructure of NIH is the hospital at the Clinical Center, and there we have great problems in hiring nurses. Nurses are becoming scarce at the salaries we are able to pay, and, in itself managing a large hospital is a complicated operation.

Let me say a word or two about research training intramurally. NIH has become one of the largest research training facilities in the world for biomedical scientists. It started in 1953 when the Clinical Center opened, and we realized it was necessary to recruit young physicians to take care of the patients. It was soon formalized into a matching program. In the last 30 years, some 5,000 physicians have spent 2 to 3 years at NIH. The physicians who come spend 30 to 50 percent of their time taking care of patients, and the remainder of their time working in the laboratories. This has been an exceptionally successful and good program, so that large numbers of our trainees are now professors of medicine, biochemistry, and microbiology throughout the country.

We also have a program for Ph.D.'s, and in the course of the last 30 years approximately 6,000 Ph.D.'s have passed through the NIH, spending 2, 3, 4, or even 5 years here. Approximately 5 percent of the young scientists and physicians who come to the NIH manage to get tenure. Most of them leave to go to universities, some to research institutes, and increasingly they are going to industry—I will say a word or two about the collaboration between industry and the NIH in a few minutes.

I should mention something about the authorizing legislation for NIH, which has been quite broad and has permitted us to establish a staff fellowship program that allows us to hire young scientists and keep them in nontenured positions for as long as 7 years, as opposed to ordinary civil-service appointments which grants tenure after 1 year. For scientists, we don't really feel that you can evaluate someone's potentiality for original research in less than several years. We take the tenure appointment, whether to a civil service position or Commissioned Officer Corps position, very seriously, we handle it very much like universities do: we write many letters, we have committee meetings, and, finally, the entire group of assembled Scientific Directors votes on the tenure commitment.

I should say something about the quality of science at NIH. There are a lot of statistical measures one can use, none of them totally satisfactory. Drs. Gee and Narin just finished a study showing that 26 percent of the papers published by NIH scientists are in the top 10 percent of papers that are quoted by other scientists (see app. 4). Scientists trained at the NIH seem to have a particularly favorable probability of getting grants, or publishing extensively. We think, by and large, NIH is a first-rate organization.

Let me say something about how we try to ensure that first-rate in terms of the review of our intramural research. Each of the Institutes has a Board of Scientific Counselors, all of whom come from outside NIH, mostly from universities. They meet two or three times a year. The work of every tenured scientist at NIH is reviewed every 3 or 4 years through a personal presentation, a review of published papers, and previous work and future plans. These reviews are then discussed by the entire group of Scientific Directors, who pay very serious attention to their recommendations about the appropriate level of support.

A word about collaboration. We have bilateral agreements with scientists in many foreign countries. The Fogarty International Center facilitates exchanges with scientists of other countries and maintains contacts with major research units all over the world.

We have always had intimate contacts with universities, where we and all of the post-doctoral scientists come from. Sometimes our people spend a year at a university; sometimes university scientists on sabbatical will spend 6 months or a year with us. We have many collaborative projects and we are an intregral part of the biomedical network.

For many years we have had some relations with industry, but not very extensive ones. But in the last few years, particularly with the growth of the biotechnology firms and change in the political climate, we have begun to have much more serious collaborations with industry. At the request of the Industrial Research Institute last year, we organized on a 2-day program for approximately 60 representatives from industry. We are planning to have another joint program this fall with the Industrial Research Institute and are expecting more and more collaboration with industry. Many of the companies have large-scale facilities which we don't have; we have some things industries don't have, and it looks as though it should be a fruitful area for collaboration.

We will be celebrating our centennial next year. The NIH began as a one-room laboratory on Staten Island in 1887, moved in 1891 to Washington, and in the late thirties moved to its present location in Bethesda. In the process of planning for the centennial we have thought about the difference between getting sick in 1887, and getting sick in 1987. One thinks of Bedlam, the insane asylum in London, where indescribable squalor and filth were endemic; and now one thinks of the surprising number of successful businessmen who have manic depressive psychoses now completely controlled, and sees the mental hospitals, the number of patients in mental hospitals decreasing enormously. I remember seeing 1,000-bed tuberculosis hospitals in the thirties and forties. They are now closed down. We still have tuberculosis, but the endemic of the 1800's and the early 1900's have disappeared. Congenital heart disease was a death sentence until 30 years ago but that is no longer true because there have been enormous advances in cardiac surgery. NIH's role in the arena of biomedical research advances started with Joseph Goldberger's discovery of the nutritional cause of pellagra, which killed some 50,000–100,000 people in the 1910's. Everyone thought it was an infectious disease. He discovered it was due to a deficiency of nicotinic acid, which could be prevented by taking a relatively inexpensive yeast extract.

A few other contributions: the discovery that fluoride prevents the occurrence of dental caries has basically revolutionized the dental profession; treatment of Wegener's granulomatosis, a very curious disease, is now quite successful, and was largely developed at NIH; improved treatment of Hodgkin's disease; better treatment of hypertension; identification of the virus that causes AIDS; identification of the virus that causes human T-cell leukemia; the discovery by Carleton Gajdusek of slow viruses which may take several decades to manifest themselves—these are a few contributions NIH scientists have made in the last three or four decades.

NIH has also made significant contributions to the biotechnology revolution. The discovery, by Marshall Nirenberg, in the early sixties, of the genetic code whereby the 4 so-called bases used two at a time can be translated into any one of the 20 amino acids which make up proteins; discovery of the enzyme ligase, which ligates DNA molecules together; discovery by Phil Leder of intervening sequences which don't code for proteins but are present in the genes;

and important work on enhancers in viruses and cellular genes—much of this has been done at NIH.

Does any type of research appear to have a greater payoff or benefit than any other? It is my suspicion that over the long haul, basic research probably has the greatest payoff. I hasten to add, however, that today, in the next 24 hours, there are going to be 500 women diagnosed as having breast cancer. There will be 500 women diagnosed tomorrow. What are we going to do with these women? If we can increase their survival from 50 percent to 60 percent, we have saved 50 people's lives each day. Clearly, we have to do something about the practical immediate problems of people who are sick. Therefore, NIH, whether it be through its intramural or extramural programs, has to have a spectrum of research projects—some aimed at trying to find out the basic biology of how cells work, and some at the clinical, applied level investigating slightly better drugs, slightly better methods of diagnosis, and slightly better methods of treatment.

A word or two about biotechnology, which has been largely discovered and developed by American scientists. It is a burgeoning industry that promises to be extremely important, particularly for the health care field in terms of all the materials which can be made: human insulin, which should not cause the production of antibodies the way beef and pork insulin does; a substitute for Factor VIII in the treatment of hemophilia, which is so difficult and expensive to extract from whole human blood; human growth hormone, which no longer will have to be extracted from pituitaries, can be dangerous because if one pituitary was from a patient with Jakob-Creutzfeldt disease, the whole lot may be contaminated with the slow virus. Some three or four patients already have died from Jakob-Creutzfeldt disease as a result of getting growth hormone derived from human pituitaries, and this can be completely obviated by using biotechnology-engineered, pure proteins. There are also vaccines for hepatitis; and for a whole variety of other diseases. The biotechnology industry, therefore, promises enormous benefits to health.

Interestingly enough, it promises, also, enormous benefits in the whole field of agriculture. Almost inadvertently, some of the research the NIH has supported has developed methods and techniques which are applicable to all sorts of agricultural problems, such as making special strains of important cereal grains resistant to insecticides, to predators, or to diseases, and conceivably engineering nitrogen fixation into non-leguminous crops. The financial benefits of this, one would imagine, down the road will be enormous.

Finally, in the remaining 30 seconds, what are the future needs? Scientifically, we need a much better appreciation of fundamental biological processes and biological control. It looks to me as though we are not going to get very many more drugs that are effective on the basis of hit-or-miss screening methods. We are going to have to tailor and exploit drugs on the basis of the peculiarities of diseases, in order to have a rational way of treating illness.

As I think Dr. Temin is going to testify, intramural NIH needs funding, just as the entire science community in the United States does. What it needs specifically is consistent and predictable funding for several reasons. One in particular we are concerned about is that young graduate students and young college students are going to be turned off if they see ups and downs in the support for research, and they see their major professors having enormous difficulty getting grants, or not getting a grant after they have been continuously funded for 10 or 15 years. Research is more or less a young person's game. If we don't have young researchers in the pipeline, we are going to be in trouble. So to borrow from Howard Temin, we need consistent, continuous and predictable levels of funding.

What are the proper roles of the public, Government, and scientists? I have no complaints whatsoever with the present roles. It seems to me eminently rational for the people to decide on priorities whether they are supercolliders in astrophysics or whether it is biomedical research, and the Congress is eminently the place in which to express these priorities. With respect to biomedical research, we at the NIH will do our best to follow the priorities you lay down.

I appreciate this opportunity to appear before you and I would be pleased to answer any questions you have.

Mr. FUQUA. Thank you very much, Dr. Rall. I think we will wait until your two colleagues conclude and then we will have some general questions.

[The prepared statement of Dr. Rall follows:]

STATEMENT OF

J. E. RALL, M.D., Ph.D.
DEPUTY DIRECTOR FOR INTRAMURAL RESEARCH
NATIONAL INSTITUTES OF HEALTH
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SCIENCE POLICY TASK FORCE
OF THE
COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES
APRIL 22, 1986

Introduction

I am Joseph Edward Rall, Deputy Director for Intramural Research, National Institutes of Health (NIH). I am delighted to have the opportunity to testify before the Science Policy Task Force today about policy for biomedical research, and in particular, how this relates to the intramural program of the NIH.

First of all, the mission of the NIH is to improve the health of the American people through research. In general, we believe that our mission requires us to study the most fundamental questions of biology and chemistry underlying disease as well as to study diseases in applied diagnostic and treatment programs. NIH is a research agency, not a medical care-providing agency. Although NIH studies diseases directly, whether they be hypertension, cancer, or AIDS, for many years we have understood that our knowledge of biological processes is so incomplete that we must mount a major effort to learn more about how living organisms, particularly human organisms, are constructed and how they function. Our knowledge of life processes is still pitifully small, but some 90% of what we do know has been learned in the last few decades. In my opinion, biological research now is moving more rapidly than any other field of science, and is the most exciting.

Management of the Intramural Research Program at NIH

In the statement of purpose describing these hearings, I count 35 questions. I will try to answer some of these as I describe how the intramural portion of the NIH works.

How is intramural NIH managed? Each NIH Institute (except for the National Institute of General Medical Sciences) has an intramural program headed by a Scientific Director. Although this official's line authority, responsibility and budget derive from the Institute Director, the overall policies and guidelines are orchestrated at the level of the Office of the Director, NIH. As Deputy Director for Intramural Research, I serve as Chairman of the assembled Scientific Directors, who meet semi-monthly to review and discuss all intramural personnel actions and issues of common concern or interest, including the external reviews of the quality of the research. In this way, the intramural programs of the various Institutes maintain comparable standards and are given oversight and guidance by the Director's office, while possessing the ability to conduct diverse research projects.

The research staff comprises about 3,500 physicians, Ph.D.s, dentists and veterinarians on the campus at NIH and we operate a 500-bed research hospital. This hospital is devoted exclusively to clinical investigation; we provide patient care necessary for good clinical investigation. We have 12 Institutes, 11 with intramural components.

What is the mix of basic and clinical work at NIH? Approximately 50% of it is basic and 50% applied research, although it is difficult to develop precise definitions.

Who sets priorities for our research at NIH? The final allocation of resources for research results from a complex interplay of many factors. In setting overall priorities, the NIH must meld scientific opportunity with broader policy considerations, including the public health importance of a disease (as measured by mortality and morbidity rates and estimates of the social and economic burden of disease), the state of knowledge in areas of science underlying the various diseases, the availability of trained manpower, facilities, and equipment to mount major initiatives, the views of various constituency groups, and the thrust of congressional mandates and special directives. Authorizing legislation, mandates, directives and appropriations also influence our research planning and the conduct of our programs. Examples include the passage of the National Cancer Act, and increased appropriations for research into AIDS and Alzheimer disease. Additionally, an important part of the priority-setting process involves the views of professional societies and voluntary health organization, the biomedical research community, and the general public. These views are sought through a variety of means, ranging from structured activities such as National Advisory Councils, special groups, or task forces or commissions to consider specific research areas or health problems, to less structured individual interaction with representatives of such groups. While these priorities tend to be rather general, we fully understand that the public who pays for this research should determine, in a rather general way, what should be emphasized. But the details of exactly how to go about it are determined largely by the scientists who do the work. A scientist who spends his life involved in some particular area of research is more likely to identify the most promising research leads and map the apparently circuitous routes sometimes required to answer important medical questions. We agree completely with the Task Force on Science Policy, which stated "strong central direction from the Nation's Capitol may be applicable in procurement policy, but may be counterproductive if applied to the government's science program." Important research tries to find the unexpected and explore the unknown, and when it is successful it often finds something that we did not expect to find. What governs cell growth and division? How does the human immune system deal with infections? What are the mechanisms involved in aging? What controls the level of blood pressure? How is fat metabolism controlled so that in some instances fatty deposits are lodged in important arteries and in other instances they are not? What are the remarkably intricate control systems that govern the reproductive cycle? The scientist who is an expert in these precise areas is most likely to have the best ideas for research into these problems.

Infrastructure

The NIH occupies a campus in Bethesda of approximately 318 acres. In addition to the National Library of Medicine, which is a library's library, we have our own library. The National Institute of Environmental Health Sciences is located in Research Triangle Park, North Carolina; a large part of the National Institute on Aging is in Baltimore, and there is a large branch of the National Institute of Allergy and Infectious Diseases in Hamilton, Montana. These 1,400 acres require the usual upkeep, managerial, policy and other services. Thus, the older laboratory buildings constructed in the late 1930s and 1940s are in need of renovation to meet contemporary safety and quality standards. We have initiated a round-robin renovation program whereby several buildings will each, in turn, be vacated, upgraded, and reoccupied.

The size and scope of the intramural program permit a high degree of interaction and collaboration between scientists of different disciplines, or different research components and Institutes. The purchase and usage of large and expensive equipment can be shared to the common advantage and purpose. Thus, we have centralized the operation and management of major projects such as the Positron Emission Tomography-Cyclotron program, and the Nuclear Magnetic Resonance Imaging and Specroscopy program.

One of the mundane but important problems for us has been procurement. In many areas of science it is not possible to foresee what experiments one should do the week after next, because the results from the experiments being done today are not yet available. This means that supplies for next week's work, or indeed, the work of the day after tomorrow, frequently have to be ordered today. Hence, it is very important that we have a quick, responsive procurement system. Fortunately, our system is reasonably well computerized. We have special mechanisms for telephone charge orders; we are particularly sensitive to paying our suppliers on time, and our own Division of Computer Research and Technology has been instrumental in developing a reasonably sophisticated data management system so that we can order responsibly and expeditiously and get the best possible prices from suppliers. These are important aspects of an infrastructure necessary for advanced research.

A very large part of our infrastructure is the management of our research hospital. This utilizes almost 700 nurses, large numbers of orderlies, clerks, cleaning people, etc., and thus requires a major effort in management and control.

Intramural Research Training

In the last quarter of a century, the intramural program at

NIH has become the largest research training facility in the world for biomedical scientists. It started at approximately the same time as the opening of the Clinical Center in 1953, when it was necessary to recruit physicians to take care of patients. It was soon formalized into a matching program for clinical associates, which has trained some 5,000 physicians in the last 25 years. Young physicians with a few years of post-M.D. training come to NIH for two or three years and spend 30-50% of their time taking care of patients and 70-50% of the time doing research in the laboratories. This program has been a major mechanism for physicians who are interested in research, but do not have the time to enter a regular Ph.D. program, to acquire, through working with a preceptor, sophisticated detailed knowledge of research and research methodology. In addition to the program for physicians, in the last twenty-five years more than 6,000 Ph.D.s have passed through our training programs as post-doctoral students. These scientists come to NIH, usually within a few years of having earned their Ph.D., and spend two to five years working in our laboratories. Although a small proportion of the younger scientists coming to the NIH in temporary positions or appointments will stay as permanent researchers, the majority of such individuals will leave to bring the expertise acquired here to the rest of the country and indeed the world. The contributions made in their later careers have spread the success of the NIH research training endeavor and attest to the quality of the training that they obtained here. While most "graduates" have gone into academic institutions, increasingly there are researchers being recruited into the industrial sector.

An important aspect of training scientists at NIH has been broad authorization language which has permitted us to set up a Staff Fellowship program. With this mechanism, we can keep M.D.s or Ph.D.s for up to seven years without a commitment to tenure. We regard the decision to offer tenure, either in the Commissioned Officer Corps or in the Civil Service, as an important one, so we solicit many letters for these candidates, and several committees debate the merits of each case. About 5% of nontenured scientists achieve tenure at NIH.

Perhaps I should make a few observations about the quality of research done by intramural scientists at the NIH. If intramural research at NIH were second-rate, everything I say about how we operate would be irrelevant. However, a recent exhaustive analysis of citations of papers published by NIH intramural scientists between 1973 and 1980 was done by Drs. Gee and Narin. It showed that more than two-and-one-half times as many scientific publications from NIH scientists as would be expected were in the top 10% of cited papers in biomedicine. This is to be compared with 1.6 times the expected average for publications supported extramurally by NIH. Another analysis of the careers of scientists trained at the NIH showed similar results: i.e., training at the NIH was associated with a considerable increase in the probability of gaining a grant 10 years later or publishing extensively. In short, objective analysis shows that intramural research at NIH is a success.

Review of NIH Intramural Research

Each Institute has a Board of Scientific Counselors of outstanding scientists drawn largely from universities. At least every three to four years they evaluate the work of every tenured scientist in each Institute, and recommend the appropriate level of support. The work of scientists who might be proposed for tenure is also reviewed. Finally, the research thrusts of the Institutes and general intramural policies of NIH are considered.

Collaboration with Other Institutions

I should say a word or two about the collaborative efforts of NIH intramural scientists. We have many bilateral agreements with scientists in foreign countries--France, Italy, Japan, Israel, etc., and there is a constant exchange of scientists, ideas and shared experiments between many countries and NIH. The Fogarty International Center facilitates these exchanges and maintains contacts with major research units all over the world.

We have always had intimate connections with universities. University professors occasionally spend sabbaticals working at NIH. Our scientists spend variable periods of time at universities when there are particular techniques or ideas which can best be pursued there. As a result, we have many collaborative projects going on.

For many years, we have had some relationships with industry, but in the last half-dozen years, as a result of the growth of research-oriented biotechnology firms and a subtle change in the political scientific climate, the number of contacts has increased. This is exemplified by a two-day symposium we arranged for members of the Industrial Research Institute in the fall of 1985, which drew representatives from about 60 companies who wanted to find out what is going on at NIH. We expect this collaboration to continue and expand, because each side, namely industrial companies and NIH scientists, has special talents and special procedures that can be combined to produce better results sooner.

Research Benefits

The National Institutes of Health will celebrate its 100th anniversary in 1987 and in thinking about this centennial, we have been impressed at the marked differences between being ill in 1887 and in 1987. Tuberculosis hospitals, which existed in most parts of the U.S., have now essentially disappeared. Patent ductus syndrome--a heart defect of infants--was able to be successfully treated surgically, but now can be treated by a drug--indomethacin. Stroke and stroke death was able to be mitigated by complicated neurosurgery, but can now be largely prevented by prescribed aspirin and standard hypertension control.

More specific NIH contributions began with Dr. Joseph Goldberger's work in the early 1900s when some 50,000 to 100,000 people died annually of pellagra. Around the late 1910s or early 1920s Goldberger identified this disease, thought to be infectious, as a nutritional disease due to a deficiency of the vitamin nicotinic acid (as it was later discovered), which was treatable with inexpensive yeast extracts. Other more recent contributions have been the introduction of fluoride to prevent dental caries (a revolution for the dental profession); better and quite effective means developed at NIH to diagnose and treat a curious and formerly fatal condition called Wegener's Granulomatosis; much improved treatment of Hodgkin's disease, a result of work both at NIH and at universities throughout the country; anti-hypertensive agents developed at NIH; the rapid identification of the virus that causes AIDS and the development of a test for it just a few years after the syndrome was first described; the discovery by Dr. Carleton Gajdusek of slow viruses which infect the central nervous system and which can take decades to manifest themselves--these are a few of the important contributions NIH scientists have made in the last 40 years.

Other aspects of basic discoveries made at NIH have played a major role in the biotechnology revolution. In the early 1960s, Dr. Marshall Nirenberg first discovered the genetic code whereby a sequence of four so-called bases can be translated into any one of the 20 amino acids serving as the building blocks of proteins. Following this came the discovery of the enzyme ligase, which is absolutely critical in putting together artificial genes; the discovery of introns, intervening sequences which do not code for proteins, but which are found in most eukaryotic organisms; and the discovery in viruses and genes of enhancers that control the activity of those genes. All these discoveries, made at NIH, have been critical to the development of biotechnology.

Does any type of research appear to have a greater payoff or benefit than other types? I suspect that over the long haul, basic research, such as that which became biotechnology, eventually has a greater payoff than most applied research, such as clinical trials. I hasten to add that, in the case of breast cancer, for example, we have no alternative but to do research on every aspect of this disease. Today and every day, approximately 500 American women will be diagnosed as having breast cancer. We must know the best way to treat them right now. If we can improve survival from 50%

to 60%, we will have helped a large number of women. Therefore, research all along the spectrum, from basic to applied, must be supported.

Biotechnology

What is the biotechnology industry doing for us? Among other things, it has produced human growth hormone, genetically engineered to be produced by bacteria. In the absence of this pure synthetic hormone it was necessary to extract the hormone from human pituitaries. It was discovered just last year that, in a few instances, some of these pituitaries were infected with a slow virus, such as the one described by Dr. Gajdusek, which causes Creutzfeldt-Jacob disease, leading to uniformly fatal dementia in only a few years. Other biotechnology products are tissue plasminogen activator, which shows every possibility of being an extremely important agent in the treatment of myocardial infarcts, or heart attacks; hepatitis vaccines, which are well on the way to development; interferon; interleukin 2, which may have a role in the treatment of cancer; vaccines for malaria; and a biosynthetic form of Factor VIII for the treatment of hemophilia. The general field of biotechnology is hardly the responsibility of NIH, but the contributions that our scientists have made are undoubtedly going to be employed in very important agricultural uses such as control of pests, control of diseases and more efficient use of fertilizers. All of these seem possible within less than a decade through the use of genetic engineering. These are substantial benefits to health and, as I have tried to imply, the financial benefits extend beyond the health field.

The Future

What are the future needs? Clearly, we need a much better knowledge of fundamental, biological processes and how they are controlled. We really do not have rational therapies for many diseases, and I think it is unlikely that we will find them in a hit-or-miss screening program. They will be found by discovering the mechanisms of disease, and with that knowledge we will then be able to devise some preventive methods or be able to attack the disease directly with specific drugs.

What should be the proper roles of the public, government and scientists? As I indicated at the beginning of my testimony, it seems to me the situation as it exists today, in which Congress interprets the wishes of the public and translates these wishes into specific authorizations and appropriations, is eminently reasonable in a democracy such as the United States. Clearly, it must be the scientists who decide on specific approaches to attack these problems. In this connection, I think it is important that the Congress not be too specific in its instructions as to precisely how these ends should be accomplished.

I appreciate the opportunity to appear before you today and would be pleased to answer any questions.

Mr. Fuqua. Dr. Raub.

[A biographical sketch of Dr. Raub follows:]

Dr. William F. Raub

Born November 25, 1939. Alden Station, Pennsylvania; married, three children.

Education. A.B., Wilkes College, 1961. Ph.D., University of Pennsylvania, 1965.

Professional history. 1965–66, Instructor/Post-Doctoral Fellow, University of Pennsylvania Medical School. 1966–1968, Health Scientist Administrator, Division of Research Facilities and Resources, NIH. 1968–1969, Acting Chief, Special Research Resources Branch, Division of Research Resources, NIH. 1969–1975, Chief, Biotechnology Resources Branch, Division of Research Resources, NIH. 1975–1978, Associate Director for Extramural and Collaborative Programs, National Eye Institute, NIH. 1978–1983, Associate Director Extramural Research and Training. 1983-present, Deputy Director of Extramural Research and Training, Office of the Director, NIH.

Professional organizations. None.

Honors, awards. Joseph Orchard Memorial Scholarship Award, Wilkes College, 1958. Dean's Scholarship Award, Wilkes College, 1961. Faculty Phi Beta Kappa Scholarship Award, Wilkes College, 1961. Summa cum laude, Valedictorian, Wilkes College, 1961. Superior Work Performance Award, NIH, 1967. Superior Service Honor Award, NIH, 1972. Quality Increase, NIH, 1974. Meritorious Award for Exemplary Achievement in Public Administration, William A. Jump Memorial Foundation, 1976. SES Outstanding Performance Award, 1981. Distinguished Service Award (Administrative), 1982. Meritorious Executive Rank Award, 1982. Toastmasters International Communications Achievement Award, NIH Toastmasters Club, 1983.

STATEMENT OF DR. WILLIAM F. RAUB, DEPUTY DIRECTOR FOR EXTRAMURAL RESEARCH AND TRAINING, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, BETHESDA, MD

Dr. Raub. Thank you, Mr. Chairman. I will direct my remarks to the NIH extramural programs; that is, biomedical research and research training as funded by grants and/or contracts.

Research grants and contracts account for approximately 81 percent of NIH expenditures. In fiscal year 1985, NIH made over 25,000 awards totaling more than $4 billion. Research grants and contracts thus are the primary means through which NIH acts to fulfill its mission.

NIH extramural awards cover many styles of investigative activity: theoretical analyses, laboratory experiments with myriad animal and plant life forms, clinical research with human subjects—both patients and normal volunteers—and epidemiological studies and field trials. About 63 percent of these expenditures are classified under the rubric basic research; applied research makes up another 29 percent; and development 8 percent.

The recipients of research grants and contracts from the NIH are a heterogeneous group of research-oriented institutions. Schools of medicine are the largest subset, receiving approximately 52 percent of these awards. All other institutions of higher education, taken together, receive about 23 percent, this includes other health professional schools, graduate schools, and undergraduate colleges. Another 25 percent or so goes to a group made up of independent hospitals, not-for-profit research institutes, small and large businesses, components of State or local government, and other agencies of the Federal Government.

About two-thirds of NIH extramural expenditures are concentrated in one award mechanism—the research-project grant. This is deliberate, for research project grants have proved to be an excellent means to support investigator initiative; and the modern history of biomedicine makes clear that research performers themselves are the ones best positioned to choose their specific research topics and approaches. Responding to such investigator-initiated ideas and relying heavily on the rankings established by peer reviewers' critiques, NIH awarded 18,219 research project grants in fiscal year 1985. In general, these projects were the ones judged highest in technical quality and most relevant to the awarding units' missions.

NIH efforts to foster and follow investigator initiative do not operate in isolation, of course. They are shaped continually by overarching strategic guidance furnished by the Congress, higher levels of the executive branch, and public advisory groups. Once equipped with consensus judgments about research needs and opportunities in their respective mission areas, NIH awarding units take appropriate steps to stimulate the cognate scientific communities. In some instances, little more is needed than to publicize the unit's goals and objectives. In other instances, more specific and more purposeful action is indicated, such as the solicitation of grant applications or contract proposals addressed to particular research topics.

Necessary though they are to fulfillment of the NIH mission, research-project grants are not sufficient. Other funding modalities must be employed in a complementary fashion if NIH extramural programs are to turn plans and priorities into accomplishments. Most prominent among these other mechanisms are research contracts, research-center grants, and awards for research training and career development. I will comment briefly about each of these.

The research contract is the means of choice when NIH awarding units wish to acquire a particular research or development product, especially one that is to be produced in accord with an NIH-prescribed approach. This funding mechanism thus is invaluable for applying existing knowledge toward practical ends, such as developing diagnostic instruments or conducting toxicity tests, or for determining the comparative efficacy and safety of health-care procedures, such as a clinical trial comparing a new drug with an established surgical procedure.

Research-center grants play several special roles in NIH programs. Some centers are focused on categorical areas such as cancer, heart disease, and diabetes. As such, they nurture multidisciplinary and interdisciplinary attacks on major health problems, and typically feature both laboratory and clinical studies. In addition, these centers often form collaborative networks and serve as agents in technology transfer, linking the research community with health care providers, medical educators, and other elements of the health industry.

Another type of center grant funds research resources, special shared facilities that enable biomedical scientists to pursue lines of research that they otherwise might find impractical or impossible. Some examples of research resources are clinical-research centers, computer facilities, and colonies of nonhuman primates. Because most NIH-funded research resources are established within institutions of higher education, these center awards are a vital part of the infrastructure that modern science, education and patient care require. Indeed, when grants for research resources are considered along with indirect cost payments and direct institutional support; that is, the Biomedical Research Support Grant, NIH funding is seen to be central to maintaining the strength and vitality of research-oriented colleges and universities.

A particularly important research resource is the National Library of Medicine, which develops and delivers health information services for biomedical scientists, health care providers, and the public at large. In addition to operating one of the most advanced libraries in the world, the National Library of Medicine is responsible for the basic medical library assistance programs that have created a national network of medical information centers. The National Library of Medicine also is a leader in supporting important research and training in medical informatics.

Equal in importance to physical infrastructure, if not more so, is human infrastructure. The biomedical science of tomorrow will be no better than the quality of the manpower development undertaken today. With that in mind, the NIH offers multifaceted programs, funding not only the training of young scientists at the pre- and post-doctoral levels but also their early, quasi-independent research endeavors. This is particularly important in new and emerging fields. In fiscal year 1985, the NIH supported 10,623 research trainees and more than 1,000 other young investigators in the final stages of becoming independent investigators. Also, recognizing the need for affirmative action to attract more minority individuals into research careers, NIH provides for substantial research participation by faculty, graduate students and undergraduate students in minority colleges and enables disadvantaged high school students to spend a summer working in a research setting.

With respect to commercialization of research results, NIH finds existing mechanisms satisfactory. The results of NIH-funded research appear routinely in refereed scientific journals and thereby are readily available for use by others, including manufacturers and forprofit service organizations. Moreover, because NIH awardees hold the first rights to the inventions their scientists produce under grants and contracts, there is considerable incentive for reporting inventions, filing patent applications, and issuing licenses that yield revenue to the awardee institution. Like other agencies of the Federal Government, NIH may obtain royalty-free licenses to use the inventions of its awardees and retains march-in rights, which can be exercised as necessary to ensure that an invention is promoted in the public interest.

Although NIH programs necessarily are oriented toward improving the health of Americans, interplay with international health activities is both inevitable and desirable. About 1 percent of NIH funds underwrite research efforts at foreign institutions. In addition, NIH facilitates the short-term exchange of biomedical scientists between the United States and other nations, and participates actively in dozens of bilateral and multilateral agreements designed to promote research and/or technology transfer in selected areas.

Mr. Chairman, in the interest of brevity, my verbal statement is limited to the foregoing summary comments. I hope they prove useful, and we will be pleased to respond to questions later.

Thank you, sir.

Mr. **Fuqua**. Thank you very much, Dr. Raub.

[The prepared statement of Dr. Raub follows:]

Statement of

William F. Raub, Ph.D.
Deputy Director for Extramural Research and Training
National Institutes of Health

before the

Science Policy Task Force
Committee on Science and Technology
U.S. House of Representatives

April 22, 1986

Thank you, Mr. Chairman, for the opportunity to participate in this hearing on "Policies for Biomedical Research." I will direct my remarks to the NIH extramural programs - i.e., biomedical research and research training funded by grants and/or contracts. My colleagues, Drs. Rall and Moskowitz, will comment on NIH intramural research and evaluation of NIH programs, respectively.

Research grants and contracts account for approximately 81% of NIH expenditures; in fiscal year 1985, NIH made over 25,000 awards totalling more than $4 billion. Research grants and contracts thus are the primary means through which NIH acts to fulfill its mission - enlarging the knowledge base for the improvement of human health.

NIH extramural awards cover many styles of investigative activity: theoretical analyses, laboratory experiments with myriad animal and plant life-forms, clinical research with human subjects (both patients and normal volunteers), and epidemiological studies and field trials. About 63% of these expenditures are classified under the rubric basic research; applied research makes up 29% and development 8%.

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About two-thirds of NIH extramural expenditures are concentrated in one award mechanism - the research-project grant. This is deliberate, for project grants have proved to be an excellent means to support investigator initiative, and the modern history of biomedicine makes clear that research performers themselves are the ones best positioned to choose their specific research topics and approaches. Responding to such investigator-initiated ideas and relying heavily on the rankings established by peer reviewers' critiques, NIH awarded 18,219 research-project grants in fiscal year 1985. In general, these projects were the ones judged highest in technical quality and most relevant to the awarding units' missions. Because the NIH system for review has been discussed in detail at a recent hearing before this Task Force, I will not discuss peer review further in this statement.

NIH efforts to foster and follow investigator initiative do not operate in isolation, of course. They are shaped continually by overarching strategic guidance furnished by the Congress, higher levels of the Executive Branch, and public advisory groups. Once equipped with consensus judgments about research needs and opportunities in their respective mission areas, NIH awarding units take appropriate steps to stimulate the cognate scientific communities. In some instances, little more is needed than to publicize the unit's goals and objectives. In other instances, more specific and more purposeful action is indicated, such as the solicitation of grant applications or contract proposals addressed to particular research topics.

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A particularly important research resource is the National Library of Medicine (NLM), which develops and delivers health information services for biomedical scientists, health care providers, and the public at large. In addition to operating one of the most advanced libraries in the world, the NLM is responsible for the basic medical library assistance programs that have created a national network of medical information centers. NLM also is a leader in supporting important research and training in medical informatics. Made possible by the advent of modern information technologies, this research endeavor is a direct response to the need to manage the growing knowledge base of biomedicine. In particular, the processes of medical decision-making and the role of information technologies therein must be explored thoroughly, for increased knowledge in this area is as important to progress in biomedicine as the fact base itself.

Equal in importance to physical infrastructure, if not more so, is human infrastructure. The biomedical science of tomorrow will be no better than the quality of the manpower development undertaken today. With that in mind, the NIH offers multifaceted programs, funding not only the training of young scientists at the pre- and post-doctoral levels but also their early, quasi-independent research endeavors. This is particularly important in new and emerging fields. In fiscal year 1985, the NIH supported 10,623 research trainees and more than 1,000 other young scientists in the final stages of becoming independent investigators. Also, recognizing the need for affirmative action to attract more minority individuals into research careers, NIH provides for substantial research participation by faculty, graduate students and undergraduate students in minority colleges and enables disadvantaged high-school students to spend a summer working in a research setting.

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Mr. Chairman, in the interest of brevity, my prepared statement is limited to the foregoing summary comments. I hope they prove helpful to the Task Force. I will be pleased to respond to questions.

Mr. FUQUA. We will now hear from Dr. Moskowitz.

[A biographical sketch of Dr. Moskowitz follows:]

DR. JAY MOSKOWITZ

Born January 9, 1943, New York, New York; married, two children.

Education. B.S., Queens College, 1964. Ph.D., Brown University, 1969.

Professional history. 1964-65, Lecturer in Biology, Queens College. 1966-67, Graduate Teaching Assistant; 1967-69, Predoctoral Fellow, Division of Biological and Medical Sciences, Brown University. 1969-71, Lt. Cmdr., U.S. Public Health Service; and Postdoctoral Research Associate, Pharmacology-Toxicology Program, National Institute of General Medical Sciences, NIH. 1971-72, Grants Associate, Division of Research Grants, NIH. 1972-73, Program Coordinator, Division of Lung Diseases (DLD), National Heart and Lung Institute (NHLI), NIH. 1973-74, Program Coordinator and Acting Chief, Special Programs and Resources Branch, DLD, NHLI, NIH. 1974-76, Associate Director for Program Planning and Evaluation, DLD, NHLI, NIH. 1976-81, Associate Director for Program Planning and Evaluation and Director, Office of Program Planning and Evaluation, Office of the Director, National Heart, Lung, and Blood Institute (NHLBI), NIH. 1981-86, Associate Director for Scientific Program Operation, NHLBI, NIH. 1986-present, Associate Director for Program Planning and Evaluation, Office of the Director, NIH.

Professional organizations. Society for Experimental Biology and Medicine, American Association for the Advancement of Science, The Society of the Sigma Xi (full member).

Honors, awards. New York State Incentive Scholarship, 1960-64. U.S. Public Health Service Predoctoral Traineeship, 1965-66. University Fellow, John G. Peterson Scholarship, Brown University, 1968-69. William A. Jump Memorial Foundation

Meritorious Award, 1977. Equal Employment Opportunity Award, 1977. NIH Director's Award, 1978. U.S. Public Health Service Superior Service Award, 1980. Senior Executive Service Performance Award, 1981, 1983, 1984, 1985.

STATEMENT OF DR. JAY MOSKOWITZ, ASSOCIATE DIRECTOR FOR PROGRAM PLANNING AND EVALUATION, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, BETHESDA, MD

Dr. MOSKOWITZ. I am pleased to be here today to describe the evaluation program of the National Institutes of Health. I have developed my testimony into two major themes. First, I will describe the genesis and organization of program evaluation at NIH; and then provide some examples of the impact of the evaluation program on science and medical practice, NIH-funding mechanisms, and research policy.

Evaluation is a major aspect of the overall NIH research program. Dr. Kirschstein testified earlier on the extramural peer review system—the fundamental evaluation system that underlies all NIH research and training support mechanisms. Dr. Berliner, and just recently Dr. Rall, described the process of review of the NIH intramural research programs, and the role played by the Institutes' Boards of Scientific Counselors in evaluating science, personnel and productivity of our intramural programs.

At NIH, there are many standing committees that conduct evaluations and assessments. For example, the NIH Director's Advisory Committee has an evaluation component that provides outside scientific and lay perspectives on major policy issues to the Director. For example, the next meeting of this committee will address the issue of "The Impact of Cost Containment Measures on Clinical Research and Research Training in Academic Health Centers." The Bureaus, Institutes, and Research Divisions of the NIH similarly have distinguished advisory councils and scientific advisory committees that continually review Institute programmatic activities and advise the Institute Directors on program directions. Thus, evaluation is considered an integral and continual part of achieving our mission.

I would now like to turn to the Evaluation Set-Aside Program. In 1970, section 401 of the Medical Facilities Construction and Modernization Amendments of 1970 amended the Public Health Service Act to establish the Evaluation Set-Aside Program. As a result of that legislation, up to 1 percent of all appropriations under the PHS Act can be set aside for program evaluation, at the discretion of the Secretary, Department of Health and Human Services. This Evaluation Set-Aside Program is administered by the Assistant Secretary for Planning and Evaluation. The Assistant Secretary establishes the Department's evaluation planning and reporting requirements, approves agency evaluation set-aside plans, and conducts its own evaluation of Department programs and policies using evaluation funds set aside from the appropriations.

At NIH, my office, the Office of the Associate Director for Program Planning and Evaluation, is responsible for administering the NIH evaluation program. Each Bureau, Institute and Division has, in turn, a designated individual responsible for evaluation activities. The centralized program includes providing assistance to the

Bureaus, Institutes and Divisions as they develop their evaluation programs, organizing collegial review of NIH evaluation proposals, developing evaluation methodologies, and conducting studies of cross-cutting issues and support mechanisms.

Since 1972, evaluation plans have been prepared annually and submitted to the Department. Mr. Chairman, I brought a copy of the latest plan for 1986 for the record (see app. 5). The plan typically includes new project proposals, reports on recently completed projects, and progress reports of those projects in process. The new project proposals are first given a concept review by an NIH Evaluation Policy and Oversight Committee comprising the BID Directors and senior staff in the NIH Director's office. These new proposals are then reviewed by a Technical Merit Review Committee composed of NIH staff selected by myself. The members of the Committee are selected for their professional expertise in the design and conduct of research, for their activities in social and behavioral sciences, and for their skills in the disciplines related to quantitative assessment. Projects are then discussed in review sessions attended by all involved in the evaluation, as well as the program staffs. Written critiques are subsequently made available to the proposers to guide them in revising their proposals, if it is necessary, and in making decisions concerning final submissions to the Department. The review process is collegial in nature and recommendations are not binding upon the submitting units. Final decisions concerning submissions are made within the individual Bureau, Institute, or Division or in the Office of the Director, NIH.

In 1984, the NIH Evaluation Program was, itself, evaluated and modified as follows:

One. Each Bureau or Institute independently designs and develops its own evaluation program. An Institute may propose or manage a project that is NIH-wide in scope. Each Bureau or Institute may establish a selection of programs for evaluation within its own domain. It is recommended that a pool of funds be established at the beginning of the year in an amount that is equivalent to that which was used historically from set-aside funds to provide an adequate and meaningful endeavor in evaluation.

Two. For the NIH-wide evaluation projects, the budget is composed of set-aside funds tapped from the BID's. The amount contributed by each of the Institutes is proportional to its appropriation of grants, contracts, and other payments, as required by the legislation. The NIH-wide evaluation program includes: studies of issues such as the organization of the NIH; biomedical instrumentation support to universities; research and training support; development of evaluation methods and measures of research activity.

The distribution principle established by the Office of the Secretary more than a decade ago for the use of evaluation funds permits the Office of the Secretary to retain up to one-fourth of 1 percent of NIH appropriations for Department-level evaluations, to make available another one-fourth of that 1 percent to the Office of the Assistant Secretary of Health for PHS studies, and to make available up to one-half of the 1 percent for NIH use for Institute, NIH-wide studies. The total expenditure of NIH funds for evaluation has always been well below 1 percent of the NIH appropriation.

Through the administrative mechanisms I have just described, financial support, technical assistance, and incentives are provided to program managers at NIH to evaluate program strategies among competing alternatives. Many evaluation efforts conducted through this authority have had significant impact on NIH operations. I am now prepared to give a few examples of how these efforts have influenced: first, internal NIH programs; second, mechanisms whereby individual Institutes support research and scientific manpower development; third, areas of science that will receive new emphasis; and fourth, research policy.

In the interest of time, I will go over just one example of each and I will submit the entire testimony for the record.

Mr. FUQUA. We will make it a part of the record.

Dr. MOSKOWITZ. Thank you, sir.

As the first example, let us consider the NIH Clinical Center. As Dr. Rall has indicated, it is a unique 500-bed research hospital dedicated to conducting clinical investigation at the cutting edge of scientific advance. A few years ago, the effectiveness of the computerized medical information system was questioned. The system is used to track all patient records, medical orders, treatment protocols, laboratory and ancillary orders, and treatment results. The Evaluation Set-Aside Program supported, first, the development of an assessment methodology, and then the execution of a comprehensive evaluation study of the information system. The results showed that while data communications capabilities were excellent in the Clinical Center, the information processing capabilities were in need of improvement. The study has guided the subsequent design, development and investment in computer system support and hardware. The resultant improvements have greatly enhanced the handling of patient information for the 1,500 registered users of the system. Our clinical scientists are pleased with the system that for the first time tracks patients easily through both their inpatient and outpatient phases of treatment and also greatly simplifies the collection of clinical drug data. This evaluation effort is an example of just one instance where new methods were needed to first design the study and then the evaluation set-aside supported the development of the needed evaluation instruments and protocols.

As Dr. Raul just described, most of the NIH budget is used to support research and advanced scientific training in the extramural settings, principally in universities and medical schools. A variety of grant mechanisms are used to award funds, each mechanism having different programmatic goals. The success of various mechanisms is occasionally assessed, and the assessment guides decisions to continue, terminate, or modify the use of the specific award mechanism. I am again pleased to provide you with an example of the influence of this evaluation-type study on a single research support mechanism.

The scientific advances of the 1960's, as Dr. Rall also described, brought effective treatment to tuberculosis and new avenues of research opportunity to pulmonary medicine. The National Heart, Lung, and Blood Institute established a new mechanism in 1970, called the Pulmonary Academic Award, to initiate the development of pulmonary academicians and to improve pulmonary curricula and training. The project, supported by evaluation set-aside funds, demonstrated that pulmonary curricula and teaching improved more at award-recipient schools than at comparison schools. The academic careers of most awardees were also advanced. The grantee institutions strengthened their existing pulmonary teaching programs to the point where they were able to sustain the effort with their own funds. The study conclusions were interpreted as indicating that this specific award mechanism, the Pulmonary Academic Award, had accomplished its objectives. As a result, a final competition for awards was announced and the program is presently being phased out. This award mechanism has, however, been duplicated to promote other emerging medical research and treatment fields such as preventive cardiology and transfusion medicine.

I have given some examples of the influence of evaluation studies on internal NIH operations and one external support mechanism. Now I would like to identify some directions in science and medical practice that have been revised using information derived with the help of the set-aside evaluation program.

The National Cancer Institute sought evidence that scientific findings from laboratory research studies were being used in clinical practice to help select appropriate therapies for breast cancer. An estrogen receptor assay, developed through NCI basic research, is believed to be able to identify women who would benefit most from endocrine therapy. It was, thus, important to provide this information to the practicing physician. The effectiveness of NCI information dissemination on this subject was demonstrated in an evaluation study and a subsequent consensus development conference which showed steady increases in the usage of the estrogen receptor assay leading to appropriate therapeutic treatment.

Some types of evaluation studies I would like to describe have a more general impact on research policy. One deals with the development of an evaluation tool which has the potential to drive policy decisions, and the other has the potential of affecting research manpower decisions.

As I have pointed out, the review process for proposed set-aside evaluation has changed recently, and we look forward to refining still further our capability of providing quality information to those at NIH who make policy decisions about the course of science and those who manage programs in support of health research.

The first program that I am going to discuss is Bibliometrics mentioned briefly by Dr. Rall. I would like to provide, if it is alright with the committee for the record the paper by Drs. Helen Gee and Frances Narin on that technique. Dr. Gee has accompanied me here today (see app. 4).

The other program that I would like to describe is on manpower evaluation. During the past several years, NIH has conducted many studies of research manpower resources and training. In conducting these studies the in-house staff works cooperatively with such organizations as the National Academy of Sciences and the Association of American Medical Colleges, and specialty groups such as the Association of Professors of Medicine.

Issues, such as the effects of research training on the subsequent careers of M.D. and Ph.D. scientists, have been explored in some depth. In general, it is apparent that the greater our investment in the research training of an individual, the greater the return we receive in terms of subsequent research performance.

The types of policy-related studies I have just described are conducted in-house with the technical assistance of outside contractors supported on contracts with set-aside funds. NIH also turns on occasion to the National Academy of Sciences to provide policy review and recommendations. Academy studies are usually supported through our evaluation set-aside funds.

The results of our studies are disseminated beyond the managers of the particular programs under evaluation.

Mr. Chairman, this concludes my testimony about the uses of evaluation studies conducted at or for the NIH, mostly supported by the 1 percent set-aside fund. I would, as would Dr. Rall and Dr. Raub, be happy to answer any questions that the Science Policy Task Force may have.

Thank you.

[The prepared statement of Dr. Moskowitz follows:]

FOR RELEASE ONLY UPON DELIVERY

STATEMENT BY

JAY MOSKOWITZ, PH.D.

ASSOCIATE DIRECTOR FOR PROGRAM PLANNING AND EVALUATION

NATIONAL INSTITUTES OF HEALTH

PUBLIC HEALTH SERVICE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SCIENCE POLICY TASK FORCE

OF THE

COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

APRIL 22, 1986

I am pleased to be here today to describe the evaluation program of the National Institutes of Health (NIH). I have developed my testimony into two major themes. First, I'll describe the genesis and organization of program evaluation at NIH; then, provide some examples of the impact of evaluation on science and medical practice, NIH funding mechanisms, and research policy.

Evaluation is a major aspect of the overall NIH research program. Dr. Kirschstein has already testified on the extramural program peer review system--the fundamental evaluation system that underlies all NIH research and training support mechanisms. Dr. Berliner's testimony described the review of NIH intramural research programs and the role played by the Institutes' Boards of Scientific Counselors in evaluating the science, personnel, and productivity of our intramural programs. At NIH, there are many standing committees that conduct evaluations and assessments. The NIH Director's Advisory Committee has an evaluation component and provides outside scientific and lay perspectives on major policy issues to the Director. The next meeting of this Committee will address the issue of "The Impact of Cost Containment Measures on Clinical Research and Research Training in Academic Health Centers." The Bureaus, Institutes, and Research Divisions (BID) similarly have distinguished Advisory Councils and science advisory committees that continually review Institute programmatic activities and advise the Institute Directors on program directions. Thus, evaluation is considered integral to achieving our mission.

I would now like to turn to the evaluation "set-aside" program.

Genesis of the Evaluation Set-Aside Program

In 1970, Section 401 of the Medical Facilities Construction and Modernization Amendments of 1970 amended the Public Health Service (PHS) Act to establish the "evaluation set-aside program." As a result of that legislation, up to one percent of all appropriations under the PHS Act can be set aside for program evaluation, at the discretion of the Secretary, Department of Health and Human Services (DHHS). This evaluation set-aside program is administered by the Assistant Secretary for Planning and Evaluation (ASPE) of the Office of the Secretary (OS), DHHS. The OS establishes the Department's evaluation planning and reporting requirements; approves agency evaluation set-aside plans; and conducts its own evaluation of Department programs and policies using the evaluation funds set aside from appropriations authorized by the PHS Act.

Evaluation at NIH

At NIH the Office of the Associate Director for Program Planning and Evaluation is responsible for administering the NIH evaluation program. Each BID has a designated individual responsible for evaluation activities. The centralized program includes providing assistance to the BIDs as they develop their evaluation proposals, organizing collegial review of NIH evaluation proposals, developing evaluation methods, and conducting studies of cross-cutting issues and support mechanisms (e.g., peer review, centers, training).

Since 1972, Evaluation Plans have been prepared annually and submitted to the Department. Mr. Chairman, I have brought a copy of the latest Plan for FY 1986 for the record. The Plan typically includes new project proposals, reports on recently completed projects, and progress reports on those in process. The new project proposals are first given concept review by an NIH Evaluation Policy and Oversight Committee comprising BID Directors and senior staff in the NIH Director's office. These new proposals are then reviewed by a Technical Merit Review Committee composed of NIH staff selected by the Associate Director for Program Planning and Evaluation. The members of the committee are selected for their professional expertise in the design and conduct of research in evaluation, social and behavioral sciences, and quantitative assessment disciplines. Projects are discussed in review sessions attended by all involved evaluation and program staffs. Written critiques are subsequently made available to the proposers to guide them in revising proposals and in making decisions concerning final submission to the Department. The review process is collegial in nature and recommendations are not binding on the submitting units; final decisions concerning submissions are made within individual BIDs and Office of the Director, NIH, respectively.

Recent Simplifications of the Approval Process

In FY 1984, the NIH Evaluation program was itself evaluated and modified as follows:

- Each BID independently designs and develops its own evaluation program; however, an Institute may propose and manage a project that is NIH-wide in scope. Each BID may establish a selection of programs for evaluation within the BID. It was recommended that a pool of funds be established at the beginning of the year in an amount equivalent to what was historically available from the set-aside and adequate to provide for a meaningful endeavor.

- For NIH-wide evaluation projects, the budget is composed of set-aside funds tapped from the BIDs. The amount contributed by each BID is proportional to the "appropriation for grants, contracts, or other payments," as required in the legislation. The NIH-wide evaluation program includes: studies of issues such as stabilization of research grants, organization of NIH, biomedical instrumentation support to universities, and research and training support; development of evaluation methods such as measures of research activity; and design and development of new data bases for program evaluation.

Evaluation Program Budget

The distribution principle established by OS more than a decade ago for the use of evaluation funds is that OS may retain up to one-fourth of one percent of NIH appropriations for Department-level evaluations, make available another fourth to Office of the Assistant Secretary of Health (OASH) for PHS studies, and make available up to one-half of one percent for NIH use for Institute and NIH-wide studies. The total expenditure of NIH funds for evaluation (NIH plus OASH plus ASPE) has always been well below one percent of the NIH appropriation.

Evaluating the NIH Program

Through the administrative mechanisms I have just described, financial support, technical assistance, and incentives are provided to program managers to evaluate program strategies among competing alternatives. Many of the evaluation efforts conducted through this authority have had significant impact on NIH operations. I am now prepared to give a few examples of how these efforts have influenced (1) internal NIH programs, (2) the mechanisms whereby individual Institutes support research and scientific manpower development, (3) the areas of science that will receive new emphasis, and (4) research policy.

As a first example, let us consider the NIH Clinical Center, a unique 500-bed research hospital dedicated to conducting clinical investigation at the cutting edge of scientific advancement. A few years ago the effectiveness of the computerized medical information system was questioned. The system is used to track all patient records, medical orders, treatment protocols, laboratory and ancillary orders, and treatment results. The evaluation set-aside program supported, first, the development of assessment methodologies, then, the execution of a comprehensive evaluative study of the information system. The results showed that while data communications capabilities were excellent, the information processing capabilities were in need of improvement. The study has guided the subsequent design, development and investment in computer system support and hardware. The resultant improvements have greatly enhanced the handling of patient information for 1500 registered users of the system. Our clinical scientists are pleased with the system that for the first time tracks patients easily through both inpatient and outpatient phases of their treatment and also greatly simplifies clinical drug trial data collection. This evaluation effort is an example of just one instance where new methods were needed to begin a study, and the evaluation set-aside first supported the development of the needed evaluation instruments and protocols.

Most of the NIH budget is used to support research and advanced scientific training in extramural settings, principally in universities and medical schools. A variety of grant mechanisms are used to award funds, each mechanism having different programmatic goals. The success of various mechanisms is occasionally assessed, and the assessment guides decisions to continue, terminate, or modify the use of the award mechanism. I am pleased to provide you with examples of the influence of evaluation findings on research support mechanisms.

A Retrospective Study

Scientific advances in the 1960s brought effective treatment of tuberculosis and new avenues of research opportunity in pulmonary medicine. The National Heart, Lung, and Blood Institute (NHLBI) established a new mechanism in 1970, the Pulmonary Academic Award, to stimulate the development of pulmonary academicians and to improve pulmonary curricula and training. A project supported by evaluation set-aside funds demonstrated that pulmonary curricula and teaching improved more at award-recipient schools than at comparison schools. The academic careers of most awardees advanced. The grantee institutions strengthened their existing pulmonary teaching programs to the point where they were able to sustain the effect with their own funds. The study conclusions were interpreted as indicating that the Pulmonary Academic Award program had accomplished its objectives. As a result, a final competition for Pulmonary Academic Awards was announced, and the program is presently being phased out. The Academic Award mechanism, however, has been duplicated to promote other emerging medical research and treatment fields such as preventive cardiology and transfusion medicine.

A Prospective Study

The National Eye Institute (NEI) was concerned over the potential for large-scale growth of its program of Core Grants for Vision Research at the expense of research project grants. An Institute-supported evaluation project was initiated to consider the program guidelines in general and the possible negative effect of Core Grants on other NEI programs. The result of the evaluation was a revision of the guidelines for the Core Grant Program. The new guidelines strengthened the requirement for collaborative efforts and dropped the previous practice of supporting new investigators and pilot studies. The increased use of traditional research grants made possible by the financial limitation on Core Grants has since strengthened the NEI research program broadly. The new guidelines have expedited the application and review process, pleasing applicants and reviewers alike, and have aided post-award management.

New Program Approaches

The National Institute for Dental Research has utilized evaluation study results to guide specific changes in research management and research directions of the National Caries Program. The caries program was evaluated with set-aside funds by a panel that considered its organization as well as the research it supported. Following the evaluation there was a restructuring of program strategies and of research approaches that permitted systemic and topical fluorides to be combined in a single treatment strategy; new emphasis was given to research related to dietary factors; staffing changes added expertise in nutrition and in analysis of cost-benefit and cost-effectiveness; and formal planning procedures were adopted. As recommended by the evaluation report, a request for grant applications was issued for cariology research centers.

Changes in Science and Medical Practice

I have given some examples of the influence of evaluation study results on internal NIH operations and on extramural support mechanisms. Let me now identify some directions in science and medical practice that have been reviewed using information derived with the help of the set-aside evaluation program.

The National Cancer Institute (NCI) sought evidence that scientific findings from laboratory research studies were being used in clinical practice to help select appropriate therapy for breast cancer. An estrogen receptor assay, developed through NCI research, is believed to be able to identify women who would benefit most from endocrine therapy. It was, thus, important to provide this information to the practitioners. The effectiveness of NCI information dissemination on this subject was demonstrated in an evaluation study and a subsequent consensus conference which showed steady increases in the usage of the estrogen receptor assay leading to appropriate therapeutic treatment.

The Anti-Epileptic Drug Development Program of the National Institute of Neurological and Communicative Disorders and Stroke has been a model for the development of orphan drugs. Managers of this program made effective use of set-aside monies to establish baseline data through a national survey of seizure rates and medications that are prescribed for drug-treated epileptic patients. These data are now being used to guide clinical trial schedules, and will be used as a baseline to assess information dissemination and future program impact on physician knowledge and practices in prescribing new drugs developed by the program.

Policy Changes

Some types of evaluation studies I would like to describe have a more general impact on research policy. One deals with the development of an evaluation tool which has the potential to drive policy decisions; and another with the potential of affecting research manpower decisions.

As I have pointed out, the review process for proposed set-aside evaluation was changed recently, and we look forward to refining still further our capability of providing quality information to those at NIH who make policy decisions about the course of science and who manage programs in support of health research.

Our evaluation program has pioneered the development and application of an objective method of measuring research activity and performance. The method, which is called "Bibliometrics," analyzes NIH-wide research program performance by assessing the quality and quantity of research journal publications resulting from NIH grant and contract support. Comprehensive analyses of publications and citations to those publications resulting from NIH extramural and intramural research support programs from 1970 to 1980 have been completed and analyses of the 1981-84 period are in preparation. Mr. Chairman, I have brought for the record a report on a comprehensive analysis of NIH intramural and extramural research publications over two four-year periods, 1973-77 and 1977-80. These studies show the extensive impact of Federal support on scientific productivity. NIH-supported research publications vary in nearly direct relation to the funds obligated for the support of research three years earlier. Our studies have also demonstrated clearly the outstanding quality of both the intramural and extramural programs of the NIH. Twenty-two percent of NIH intramural program research publications are in the top decile of cited papers, and fifteen percent of extramural publications can claim this distinction. We have only begun to track changes in publications over time and to relate these to changes in NIH policies.

We believe that this type of analysis can be used to alert us to fields that warrant increased attention from the NIH and can help also to identify areas in which decreased support may be in order. Much can be learned about the changing course of biological science by examining the scientific literature from a global perspective.

During the past several years, NIH has conducted many studies of research manpower resources and training. In conducting these studies in-house staff work cooperatively with such organizations as the National Academy of Sciences, the Association of American Medical Colleges, and specialty groups such as the Association of Professors of Medicine.

Issues such as the effect of research training on the subsequent careers of M.D. and Ph.D. scientists have been explored in some depth. In general, it is apparent that the greater our investment in the research training of an individual, the greater the return we receive in terms of subsequent research performance.

It is evident that two to three years of postdoctoral research training is essential to allow a clinician to become a competitive investigator. This occurs in our intramural and extramural fellowship program with a high degree of success. Our studies suggest that we might improve the efficiency of our manpower development investment through policy changes urging increases in the length of training programs. Other mechanisms, such as the Physician Scientist Award, affording longer periods of career development support, have also been developed, partially as a result of our evaluation studies.

The types of policy-related studies I have just described are conducted in-house with the technical assistance of outside contractors supported on contract with set-aside funds. NIH also turns on occasion to the National Academy of Sciences for policy review and recommendations. Academy studies are usually supported through our evaluation set-aside program. Examples of such Academy studies are (1) the recent analysis of NIH organization and structure, (2) studies of needs for and alternatives to animal models in biological research, and (3) reviews of the status of and current issues in various areas of biomedical research.

The results of evaluation studies are disseminated beyond the managers of the particular programs under evaluation. Copies of all reports are filed in the PHS Evaluation Documentation Center. Many are distributed throughout NIH. Some, such as the NAS report on personnel needs, are printed and mailed to the biomedical community. The Science Policy Research Division of the Library of Congress receives copies of many reports. The National Technical Information Service archives all reports on microfilm and produces hard copy at cost. We understand that over two dozen copies of the six-volume Clinical Center Management Information System evaluation have been purchased from NTIS.

Mr. Chairman, this concludes my testimony about the uses made of evaluation studies conducted at or for NIH, mostly supported by the "one-percent" set-aside fund. I would be happy to answer any questions that you or members of the Science Policy Task Force may have.

PANEL DISCUSSION

Mr. **Fuqua**. Thank you, gentlemen, all of you, for very, very informative testimony this morning. It has been very helpful. And of course, NIH has a very excellent track record, and whatever you have been doing must have been somewhat right based on the results.

Dr. Moskowitz, how are you able at NIH to carry out and implement evaluation studies in such a manner that the management and staff of those being evaluated do not become hostile or take an interest in the study and try to certainly make such changes as may be recommended? And do they accept those recommendations that are made to them, that are in their best interest?

Dr. **Moskowitz**. In 1984, we went through an evaluation program assessment, and as a result of that we have set up a two-tier system. The first tier, the Evaluation Advisory Committee, is set up using Institute Directors, the people who are in charge of running the programs for the National Institutes of Health. They review proposals that are submitted in concept. So at the first line, we have the person who is in charge of carrying out the mission of that Institute reviewing the concept of the evaluation proposal.

That is a collegial review as well. We provide the proposals for the evaluation to this group in advance; they have a chance to talk it over with their staffs, and then they come to a meeting, which happens once a year—in fact, it will be taking place in a few weeks from now for this year's plan—and they discuss, critique the concept and decide whether it will carry out the mission of their particular Institute.

As a result of that advisory committee review, those proposals that are "approved," let's say in quotes, are then moved down to a next review, which is a technical merit review. Here again, as I have described, we bring in experts in evaluation methodology from NIH, and provide a chance for the person who proposes the evaluation study to discuss it with his or her peers at NIH and get constructive criticism.

These kinds of collegial reviews help to temper any hostility that might originally develop if someone was criticizing a specific program. There is a lot of back and forth, and it is in the best interest of the person who is proposing the study to accept the advice of their peers. We have found it works very well.

For example, the evaluation of the Pulmonary Academic Award Program, that I described, had been discussed not only with the person who was in charge of the Pulmonary Academic Award Program but also with Pulmonary Academic awardees at the universities. The scientists themselves and the researchers themselves are interested in developing a study that will suit their needs best and attain their objectives. In that particular program, which I can speak about indepth about, because I developed the Pulmonary Academic Award Program and its evaluation, there was a very collegial review all the way up from the university, the Institute Director and the person who was doing the evaluation. And this example, also serves as a model for other kinds of evaluations.

Mr. **Fuqua**. Well, I was going to ask you, is there a model that has been developed that could be applied to other agencies in trying to evaluate scientific proposals, or also maybe even to Congress as we are trying to evaluate scientific programs? Not the specific but in the broad sense, like if we wanted to evaluate NIH or NSF or DOE, or some of those agencies.

Dr. MOSKOWITZ. Our programs are so diverse and so different that there is not one specific model that can be used to evaluate each of our programs. Each one requires a different approach. Each one has different criteria. For example, I could use the one I just mentioned, the evaluation of the Pulmonary Academic Award Program, in part, to evaluate other academic award programs and possibly other career programs, but that model could not be used to evaluate a center's program or Dr. Rall's intramural program. We would have to go to a different methodology. We use different so-called models for developing different sets of programs. But I can't think of any specific model that could be used for looking at the overall NIH Program.

Mr. FUQUA. Dr. Rall, with the exception of the Institute of General Medical Sciences, most research at NIH is conducted by disease or that type of category. What level of coordination exists among the Institutes with the respect of changing information or setting research priorities or developing joint programs—I think you mentioned interdisciplinary research—and trying to avoid duplication of those efforts?

Dr. RALL. This is an important point, and one we are concerned about. At the top there is coordination through the meetings of the Scientific Directors of the various Institutes where we discuss varied and assorted problems, opportunities, and so forth. At probably the more important working level, people have their own groups. The immunologists, for example, in the Cancer Institute, in Allergy and Infectious Disease, in Diabetes—in most of the Institutes—have their own journals, clubs, and seminars, and have set up a series of courses to be given to young people interested in immunology. They serve as a coordinating body in a very informal way for anyone interested in that discipline. We are always concerned that someone in building 2 isn't going to know what is happening to someone in building 36, and they should get together. We are trying to accomplish this exchange in many different ways. For example, we are planning an NIH Research Day this fall when the entire day mostly will be devoted to making sure that the young scientists meet each other and meet some of the more senior scientists.

Mr. FUQUA. I am also thinking about, in some of the treatments that may have carryover effects into some other area, that there is a proper coordination to make sure that you are not causing a worse problem by trying to treat, maybe, one problem.

Dr. RALL. That is always a problem. I think it was L.J. Henderson who said, somewhere around 1905, or 1910, that it was only in about 1905 that the average patient with the average disease meeting the average physician was better off for the encounter. We are concerned about that. But there is a Medical Board with representatives from each Institute advisory to the Clinical Center that meets every week or two, and there are extensive reviews of the protocols and extensive interchange between the various Institutes. Also, each Institute generally provides some clinical service to all patients. For example, the Cancer Institute provides the general surgeons who do surgery for all the Institutes; the Diabetes Institute provides gastroenterologic consultation and endoscopy for all the Institutes; the Heart, Lung, and Blood Institute has cardiologists, because people with all sorts of diseases get heart disease—and so there is a constant interchange. We have a feeling that in the clinical investigative area we have as good a coordination as it is possible to have.

Mr. **Fuqua**. I think you cited that scientists trained at NIH have an increased probability of obtaining a project grant later in their career. Is this because they are better informed, or is this because they have buddies at NIH that can look after them? How much weight is given to the fact that somebody has been NIH trained?

Dr. **Rall**. I don't really think, sir, any of the above. Usually at a university, the researchers know much more about grants than you do if you are at the NIH, because your professor has one, your friends may have one, and you are constantly writing grants proposals or discussing them.

The question of buddies always comes up and there is always worry about the old boy network. I think the peer review process does about as well as can be expected to try to prevent that from happening.

It is quite possible that the reason the people who were trained at the NIH do so well both in achieving grants and in publishing a lot is that probably the best people came to the NIH. It is not necessarily clear that we had much to do about it.

Mr. **Fuqua**. Maybe some of it rubbed off.

Dr. **Rall**. We hope so.

Mr. **Fuqua**. Dr. Raub, you talked about, or it has been talked about, the stability of individual project grants, that they could be improved by increasing the grant periods. We have had other testimony to that effect. Have you done this for first-time awardees?

Dr. **Raub**. Yes, sir, we have, as well as for individuals in midcareer who are judged to be outstanding in both their achievements and their future prospects. And just as your question indicated, we viewed it as a desirable, if not necessary, improvement to the project grant system that would give individuals a greater degree of stability and predictability in terms of their funding relationship with the NIH.

Mr. **Fuqua**. Are you satisfied with the accountability that you get from these extended periods, particularly when you have to come up and visit Dr. Natcher once every year?

Dr. **Raub**. Yes, sir, we are just now beginning on it, and so by definition, we don't have anywhere near the corpus of data to establish definitively that accountability is adequate or not. However, the approach has been rooted very carefully in our traditional procedures and among other things we have been mindful of the concerns expressed by other committees of the Congress with respect to adequate oversight and accountability. We are confident that the design we have will simultaneously foster that greater stability while still giving us the oversight and accountability we need.

Mr. **Fuqua**. Let me say that I was being somewhat of a devil's advocate in asking the question.

Dr. **Raub**. I was hoping you were.

Mr. **Fuqua**. I think it seems to me to be appropriate to try to extend those times. But at the same time, we still must try to be accountable, particularly when we are still on the annual budget cycle of that. What proportion of your first-time grants funded by NIH goes to those well-established institutions with large, ongoing program grants?

Dr. **Raub**. I don't have a precise figure at my fingertips, but the distribution of first-time grants tends to be a pattern similar to the overall distribution of NIH awards. Like most other research agencies that depend heavily upon academic institutions, our patterns of funding tend to follow the distribution of the research-intensive institutions geographically, and so therefore there are heavy concentrations of investments in the east coast, and the west coast, and the upper midwest.

Mr. **Fuqua**. One final question. How does the National Library of Medicine, the availability of it to your extramural researchers—do they have to come here to utilize those facilities or is it available on a computer network to their own? I was going to ask Dr. Moskowitz if there has been any evaluation of that. Is it being utilized?

Dr. **Raub**. Yes, sir, it is. Both the options you mention exist and, in addition, there is the network of regional medical libraries for which financial and technical assistance is anchored in the National Library of Medicine. As a result of that, an individual scientist in the extramural community first, through his or her own local library, may gain access online to extensive files of bibliographic information via computer, and may also request a variety of interlibrary loans and other services where hard copies of documents, especially hard-to-get documents, are required. When the local library is not sufficient, the regional library generally is the means of choice. And last but not least, the NLM, itself, with its unique collection in Bethesda or its international contacts is usually able to identify and supply desired documents. We believe it is a very effective service. I am not aware of formal evaluation studies in very recent years, but over time there have been several assessments of the NLM, each one giving it high marks as the premier biomedical research library in the world.

Mr. **Fuqua**. Dr. Moskowitz.

Dr. **Moskowitz**. There are, in fact, many programs of the Library of Medicine being evaluated presently, and may have been evaluated in the past. For example, the Library of Medicine has a research project grant program of its own which deals with libraries, and that has been evaluated. As far as people outside using computer networks like CHEMLINE and MEDLINE, the various programs they have for abstracting information on chemicals and various diseases, those are also evaluated, and we have an assessment of the CHEMLINE actually going on right now. So the answer to your question is yes, the Library's programs are evaluated. And in the document that I have provided for the record is an outline of the five that are presently ongoing (see app. 5).

Mr. **Fuqua**. I would like to recognize Mr. Walgren, and before to say that not only is he an able chairman of the Science, Research and Technology Subcommittee of this committee, he also serves on the Health Subcommittee of the Energy and Commerce Committee and the only Member of Congress that I am aware of that serves on both of those subcommittees. He chairs one and is the senior member of the other one, and, of course, in his own right he is a very distinguished Member of Congress.

Mr. **Walgren**. Thank you, Mr. Chairman.

I wanted to ask about the indirect costs controversy and what your view is of the obligation of us in Government to fully reimburse what are real costs, and what your abilities as administrators are to recognize some costs and perhaps not honor others so that we could be assured that there isn't at least certainly frivolous abuse of that obligation on our part to reimburse costs.

Dr. **Raub**. Mr. Chairman, the NIH believes that the indirect costs issue deserves every bit of the controversy surrounding it because it is so important—important both to the health and stability of those research institutions, especially institutions of higher education, as well as to the importance and the continuation of our programs. We recognize indirect costs as real costs, and therefore not only a legitimate but necessary element of providing the milieu in which the research is done. But we also recognize that there is so much uncertainty about some elements of the costs, especially where research butts up against the traditional educational functions of those institutions or certain of the service functions, that there must in all of our interests be a greater clarity and better definition of what constitutes an appropriate indirect cost and what doesn't.

We believe that the recent recommendations from several quarters, including the Office of Science and Technology Policy, are a major step in the direction of highlighting those areas of uncertainty and mobilizing the common interests of the Federal agencies and the research institutions, especially universities, to finding some common ground in defining a reasonable base for indirect costs. Then policies should be developed that will ensure that research institutions have the recognition and the stability of funding that is in the interest of both the universities and of the Government agencies.

Mr. **Walgren**. Do you enter into a negotiation with the university when you ask them to carry out a research project that would specify what costs you are anticipating and what you might not recognize as appropriate?

Dr. **Raub**. At the time of making an award, whether a grant or a contract, the NIH does go through a negotiation with the appropriate officials representing the institution. Typically that is the principal investigator/scientist. It may or may not include a business official. However, those negotiations are restricted to what we call the direct costs of the research. We do not include in those negotiations a consideration of the indirect costs, and that is because those indirect cost rates are established by another component of the Department of Health and Human Services. It is, therefore, NIH's policy and practice to honor those negotiated rates as given to us.

Mr. **Walgren**. What other component is that?

Dr. **Raub**. There is a unit within the office of the Assistant Secretary for Management and Budget concerned with grants and procurement that is responsible for the network of regional negotiators who work routinely with the universities and other institutions to establish the indirect cost rates.

Mr. **Walgren**. I guess what is troubling me is do you feel that we should go to some kind of flat percentage that does not recognize real cost? Obviously a flat percentage cannot. Couldn't we rely on an individual negotiation? Because at that point the Government is clearly voluntarily recognizing the legitimacy of costs that are anticipated to be presented. It seems a little difficult for me, after we voluntarily recognize legitimacy of costs, to come back after it is done and say, "Oh, but somehow or other something frivolous got in there and our only recourse now is to go to a flat percentage basis that does not reflect real costs."

Dr. **Raub**. The NIH, and I believe most other agencies, would be leery about, as you put it, a flat rate for indirect costs overall that does not cover recognized real costs. The current proposal under debate is much more circumscribed than that. It focuses on that one part of the indirect cost pool that has been not well defined, that is most controversial, and that by many analyses has cost elements that are seen, if anything, as more appropriate to the nonresearch functions of the university. The proposal, therefore, is to be much more precise, and define via a fixed rate the one element of indirect costs that has defied satisfactory uniformity in the negotiations to date. But I believe there is no intent on the part of the Department of Health and Human Services or the other entities, such as the Office of Naval Research or the Defense Contract Audit Agency, to change the fundamental approach to individual negotiations that establish those indirect cost rates that then are honored by all of us as we make awards.

Mr. **Walgren**. Let me ask you, in thinking about the peer review system, and where there may be a role for the administrators of these funds to push an area of research perhaps a little bit harder than the peer reviewers—well, perhaps I state that wrong. To what degree do you as an administrator direct funding into areas that have greater potential delivery and in that sense push the science, I guess, a little bit beyond where the proposals are coming in because there is a greater potential benefit in that?

I think, for example, the thing that brought this to mind was that my area has a resuscitation center where someone is trying to do basic research in resuscitation at the near-death period or situation. The worse thing we can do, of course, is half resuscitate somebody. In fact, our technological powers are clearly strong enough to have that be the case, and we are then saddled with all the costs of having brought somebody back but not really back to any functioning state. And the argument apparently is that if we could push that area a little bit more we would then be able to bring many more of these people back to a functioning state, rather than a state where they are neither functioning nor not functioning.

Now, if that is true, assuming that were true, this is an area that could yield some real benefits if we were able to push it back 5 minutes or so. And yet there is no ability to bring attention to that because the sciences involved are all cross-disciplinary, and no one is all that interested in that area. They are interested in bits and pieces of it, but they are not focused on that as a goal. So the question is how do you as administrators look across the board, and single out areas that might have some greater potential benefit and then try to push that science in that area?

Dr. **Raub**. In my prepared statement I used somewhat cryptically two terms of art for the NIH: one is technical merit, and the other is program relevance. Those considerations, and sometimes the tension between them, I believe, go to the point that you just raised. From the earliest days of the NIH extramural programs there was the recognition that, from time-to-time, there would be diverse points of view as to what was appropriate to push and perhaps different weights assigned to the scientific and technical quality of a particular activity, in contrast to what might be seen to be its medical or its social import if it could be pursued successfully. Therefore, somewhat like the separation of powers in the Constitution, the NIH designed its administrative system to allow for the expression of these different perspectives, and also to create some healthy tension among them.

First and foremost, we set up the peer review in such a way that the management of that assessment of technical merit is carried out by staff who are totally independent and separate from those who will make ultimately the funding decision. Therefore, it gives us the opportunity early in the process to have the assessment of scientific and technical quality of the proposed activity made ideally without any consideration of such things as the program relevance, the amount of other activity in the field, the potential medical or social significance, and the like.

As a human institution, it frequently falls short of perfect, but we believe it works in an excellent way in giving us at the first stage that unvarnished and uninfluenced consideration of what the scientific and technical merit of this idea, or of this plan is.

Second, the peer review system has two steps in it. First is the assessment by peers of the technical merit. The second is the consideration by what we call the National Advisory Councils and Boards. The Councils and Boards, by definition, are approximately two-thirds scientists and about one-third lay persons. The Councils and Boards have the responsibility not only to look over the recommendations of the first group, but to bring to bear the broader array of judgments such as "Is this an area that is ripe to be pushed?" even though a somewhat more narrowly construed scientific judgment might be tempered about it. The National Advisory Council, therefore, has the right and the responsibility to recognize that on certain occasions the scientific and technical consideration should be supplemented by views as to what is important to the program mission. This deliberation may include anything from a perception of a unique opportunity, to the recognition that there is no other project ongoing that deals with the particular subject at hand, and therefore the Institute's program would be better balanced if this were included.

Those recommendations then all converge on the Institute Director and his or her senior staff, and it is those individuals that have the responsibility to synthesize all those perspectives and express it through their funding judgment. We believe that, in the main, we have a consistently successful system that helps us ensure that those different points of view come to the surface and are considered at funding time.

Mr. **Walgren**. Can you tell a little bit more about how those Councils function? Do they function independently of the proposals that are submitted? Are they meeting and looking over the range of opportunities in an area?

Dr. **Raub**. The Councils meet typically three times a year, tied into our application cycle. Their meetings are driven by the flow of applications, in that under legal requirements a Council or Board must recommend approval of any given grant application before we may fund it. Therefore, the Councils are a necessary part of the two-step peer review process.

The Councils, however, are not limited in their function to the second-stage review of grant applications. They are the principal and senior advisory group to the Institute Director and his or her staff with respect to the goals of the larger program and the expression of the priorities for that program. Therefore, the Councils become very important advisers in taking grant applications as they come through the system accompanied by the judgments of scientific and technical merit that have been added by the first stage of peer review, and then creating a synthesis in their recommendations for funding.

Mr. **Walgren**. Are their proceedings open in their reviews of the areas and the potential of areas?

Dr. **Raub**. The Council proceedings with respect to overall missions and approaches and priorities are open meetings. The only parts of Council meetings that are closed are where the actual grant applications are on the table being discussed one by one.

Mr. **Walgren**. And is there a transcript of that discussion and that is available to the scientific community and to Members of Congress and the like, so we know what the discussion of the priorities is like that the administrator is then receiving?

Dr. **Raub**. There generally is not a transcript in the sense of a verbatim account of the Council meetings. For the part that involves grant application review, there is a thorough and a stylized tabulation of the Council's votes and recommendations that does become available. In addition, in those areas that are open to the public—which is the bulk of the Council's substantive business—there generally is some kind of accompanying documentation beyond the minutes, typically in the form of reports on program planning generated with the aid of sometimes hundreds of scientists and lay persons around the country, and at other times evaluation studies such as those Dr. Moskowitz described.

I believe Dr. Moskowitz has a supplementary comment.

Dr. **Moskowitz**. I was going to add that in addition to the grant review process and the discussions that go on at the Advisory Council that Dr. Raub has talked about, there is also another process in the planning functions of the individual Institutes. In this process—if I could use the Heart, Lung, and Blood Institute as an example, since I have just come from there less than 3 months ago—there are two phases of planning, one which uses scientific advisory committees, which are non-Government employees who are at the forefront of different areas of research, and come together to discuss the timeliness and scientific efficacy of specific projects. Now something like resuscitation centers and cardiac resuscitation may come up at the Cardiology Advisory Committee. It will compete against other initiatives that are brought up, for example, looking at drug therapy for patent ductus asteriosus or some other areas of prevention of stroke. All these areas are discussed in an open meeting and these initiatives are put into a priority-type order which are then recommended to the Institute staff, which are then moved up to the advisory committee, or council.

The Advisory Council, in addition to discussing the issues that Dr. Raub has talked about, also reviews for the next 2 years the kinds of initiatives that might be at the forefront of preventive medicine or treatment or therapy. So there are two mechanisms that are occurring at the same time, all ending up at this Advisory Council meeting.

Mr. WALGREN. Let me ask just one other question, and that is in this peer review process. Do you do things like drop out the lowest evaluation and drop out the highest and strike an average? How do you reconcile the fact that different reviewers would look at something differently?

Dr. RAUB. The current practice, in fact, one that has been maintained for many years, is to rely first and foremost wherever possible on the discussion of the assembled group, rather than do reviews by the mail or by the telephone, in any disconnected way. It has been our experience that having that discussion around a table somewhat similar to this one does more to get issues, especially differences of opinion, clearly defined and to give the group some chance to deal with the difference.

Once the group is ready to vote, each member provides a score and those scores are averaged. We have experimented from time to time with different variations on that procedure including dropping the high and low scores. The judgments of those who carried out those trials were that it did not make any material difference in the ultimate ratings, and so therefore we have not adopted any such procedures over and beyond the simple averaging of the individual scores.

Mr. WALGREN. Thank you, Mr. Chairman.

Mr. FUQUA. Gentlemen, thank you very much for sharing with us this morning your views. We again thank you for readjusting your schedule to come in early.

[Questions and answers for the record follow:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

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July 30, 1986

The Honorable Don Fuqua
Chairman, Committee on Science and Technology
Suite 2321, Rayburn House Office Building
U.S. House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

Thank you for giving me the opportunity to testify before the Science Policy Task Force on April 22, 1986, and to answer some supplemental questions for the record of the hearing. My answers are enclosed.

Please let me know if I may be of any further assistance.

Sincerely yours,

J. E. Rall, M.D., Ph.D.
Deputy Director for
Intramural Research

Enclosure

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COMMITTEE ON SCIENCE
AND TECHNOLOGY

Supplemental questions and answers for the hearing record, Science Policy Task Force, April 22, 1986

1. You indicate that both basic and applied research must be supported because of the necessity to deal with health problems in the best manner possible now while working on better, more efficacious solutions. What is the present balance between basic and applied research programs? Does this fluctuate and, what are the determining factors? In your view, what is the proper balance?

It is never easy to determine the correct balance between basic and applied research because it depends to a great extent on the precise definition of the words "basic" and "applied." In general, approximately 60% of the research NIH does or supports is basic and the remainder is applied, with the caveat that sometimes clinical research is very basic in nature, and sometimes laboratory work is applied, so another assessment of the same research projects might arrive at a different ratio between the two.

The ratio between basic and applied research does fluctuate, but not very much. Even in an emergency, such as the current situation with Acquired Immunodeficiency Syndrome (AIDS), a great deal of clinical and applied research is required, but simultaneously, much basic research is necessary to investigate the nature and mode of operation of these unusual viruses. Hence, even in extraordinary circumstances there is still more or less the same ratio between basic and applied research.

It is very difficult to say what the proper balance between the two is, because it is clearly necessary to bring basic science discoveries into applications, so applied research is necessary at some stage in the development of most important discoveries. We have patients who are ill with a variety of diseases and to make sure they are getting the best treatment it is necessary to do the most applied kind of research.

2. It is generally recognized that clinical research is important for the transfer of basic research information to clinical practice and for the evaluation of new therapeutic strategies. Is clinical research becoming more costly to perform at the NIH? If so, can you offer any solutions or recommendations for the short-term? for the long term?

Clinical research is indeed becoming more costly to perform, not only at NIH but throughout the country. One of the reasons for this is the tremendous increase in the technology now available in the clinical practice of medicine, represented by procedures such as computerized axial tomography (CAT scans) and by magnetic resonance imaging (MRI). With the latter, the instruments cost one to three million dollars. Positron emission tomography (PET scanning) is even more expensive; to produce the short-lived isotopes usually requires a cyclotron, which can cost one to three million dollars, and the instruments themselves cost around one million dollars apiece. The enormous breakthroughs in imaging and in diagnosis require commensurately more expensive technology. I am not sure that there are any solutions to the problem in either the short or the long term. In the long term, it seems likely that a balance between the new technologies will gradually evolve so that we will know in which situations it is better to have an MRI image or an ultra-sound image, or a PET or a CAT scan, so we will be less likely to use all of these modalities. Furthermore, many of the new modalities will replace older and more costly procedures, i.e., CAT and MRI imaging now frequently supplant pneumoencephalograms, a painful, somewhat dangerous, and very expensive procedure. Having said this, however, I must note that undoubtedly in the next ten years there will be newer and perhaps even more expensive machinery developed which will be important in the practice of medicine, so I am not sure that there really is any solution to the problem of expense.

3. You cite the recent initiative at NIH with respect to joint programs with industry in the field of biotechnology. In your view, what are the advantages and disadvantages of this initiative for the short-term? for the long term? Will it occur in other research areas as well?

As I see it, the advantages of this collaboration are that industry and NIH have special areas of expertise and solutions to important problems are going to be found more quickly if both players in the arena cooperate rather than going their separate ways. Clearly, there are some areas in which industry is better set up for large-scale, costly and complex procedures, whereas the NIH may have expertise in the basic sciences. I suppose the disadvantage of such a cooperation would be if either were to become subservient to the other. We at the NIH have been particularly concerned not to act as a handmaiden of any particular industry or company, and so far, I have not seen any evidence to indicate that this has happened. It is hard to predict whether there will be a big increase in collaboration between NIH scientists and industries in other research areas, but I suspect, with the present political climate and with the increasing complexities of biomedical research, that we may well find that scientists at the NIH will engage in more active and prolonged collaborations with industries spanning a wide range of different fields.

4. In the event that funding is to continue to be practically level for a period of years, how can priorities be established? Have there, in the past, been instances where a line of research was discontinued and the resources devoted to new and higher priority areas? Is this going to have to become a more prevalent practice, in your view, in the future?

Assuming level funding for the NIH, priorities must be established. In general, this means identifying and supporting those areas and, in particular, those people who are doing the most innovative and important research at the expense of other areas where there are fewer opportunities, or scientists who seem to be less innovative. There have been instances in the past where a line of research has been discontinued. I remember not long after cortisone was discovered and it was extremely difficult to synthesize, that NIH had a laboratory section working on the synthesis of corticosteroids. By the mid 1960s, once the synthesis problem was more or less solved, the section was discontinued. There was another laboratory dealing with membrane transport from a biophysical standpoint which was discontinued, in part because its chief retired and in part because membrane transport research had taken a different direction. With level funding I think reallocation of resources is probably going to become more prevalent--that is to say, more laboratories will be abolished or reduced in size so that more productive laboratories can be supported adequately. I should point out that this cannot be done overnight. If a laboratory is to be abolished, one has to be consider the personnel doing the work. In general, it is difficult and undesirable to discharge scientists who are, in point of fact, competent, therefore other laboratories have to be found where they can be useful. Although it is possible to abolish laboratories and change emphases, care and planning are required.

5. From your perspective, can you estimate the adquate level of funding needed to maintain the momentum of NIH's research effort and productivity? Should there be a stable funding level so that progress is not jeopardized?

It is very difficult to estimate the level of funding needed to maintain NIH's research effort and productivity. Clearly, if we do not have available a constant amount of resources suitably adjusted for inflation it is going to be very difficult to maintain much momentum, for three reasons. One is that the increasing complexity of science makes it more expensive to perform. Much of the newer science is very labor-intensive, and requires very skilled labor. We can no longer depend on college graduates to do many of the routine procedures, because there are fewer routine procedures. Frequently Ph.Ds., M.Ds. or people with equivalent knowledge and experience are necessary. Secondly, the cost of high-technology equipment and technicians has increased. Finally, overall morale and perception of the research climate in the university community is particularly important. If funding decreases college students will see major professors losing their support and will be less interested in pursuing a research career. In the long run, this is probably the single most serious consquence of a reduction in funding, because its effects will become apparent very quickly to students in universities throughout the country who may decide that a career in medical research is not for them. If science loses some of these brightest minds it will have lost a substantial fraction of a generation's research.

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July 30, 1986

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COMMITTEE ON SCIENCE
AND TECHNOLOGY

The Honorable Don Fuqua
Chairman, Committee on Science
 and Technology
U.S. House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

Thank you for your kind remarks about my April 22 testimony before the Science Policy Task Force, and for offering the opportunity to supplement the hearing record with additional background for the Science Policy Study Report. I am pleased to be able to respond to your questions.

1. From your perspective, are different styles of funding and management better suited for particular fields of science or researchers? Does a certain type of research support, i.e., individual project grants, center grants, result in a greater technological payoff in terms of medical products or improved health care? Are there any data to address this question from the view of the cost-effectiveness issue?

Experience suggests that different funding and management styles do, indeed, correlate to a considerable extent with different aspects of scientific and technical activity and different needs of researchers. For instance, individual efforts in basic research generally are best funded under individual research project grants; targeted research and clinical studies are often better performed under cooperative efforts or as part of program project and center grants; and more advanced stages of application (development and demonstrations of preventive and therapeutic drugs and devices, for instance) are well accomplished with the more substantial participation of NIH staff under cooperative agreements and contracts. While I know of no definitive data addressing this question from a cost-effectiveness standpoint, it is critical to ensure that all these extramural funding and management mechanisms be available to program leaders to accomplish diverse goals in the best possible fashion.

2. You indicate that research grants and contracts account for approximately 81 percent of NIH expenditures with over 25,000 awards totalling more than $4 billion in Fiscal Year 1985. How does this compare with the past few years and what do you envision for the foreseeable future (next 5 years) given the current funding constraints?

Over the past ten years NIH extramural awards have accounted for 79-83 percent of total NIH expenditures, and in Fiscal Year 1985 totaled $4.2 billion, or 83 percent of the NIH budget. Given the many current and pending perturbations in the system it would be difficult to predict future trends in allocations between extramural awards and internal research and management. For instance, while relative apportionments might stay fairly constant for continuing extramural and intramural functions, allocations for special internal needs, e.g., alterations, renovations, and construction, could add to that portion of the NIH budget, whereas reductions for those functions would tend to maintain higher proportions for extramural funds.

3. What proportion of the extramural grants are center grants versus project grants? How has the proportion changed over the last few years and what do you see for the future? What factors determine the proportion of support for each? In your view, what is the proper balance?

In Fiscal Year 1985 NIH awarded $485 million for center grants, representing 12.1 percent of NIH extramural research awards, contrasted with $2.177 billion for individual research project grants (54.3 percent) and $605 million for program projects (15.1 percent). While the dollar amount for center grants had approximately doubled from $246 million in Fiscal Year 1976, the proportion dropped slightly from 14.6 percent. This drop in the center grants portion resulted largely from an emphasis in the early 1980s on maintaining the investigator-initiated research project grant base, even at the expense of other types of award mechanisms. While some stable balance point may now have been reached, future trends will depend primarily on various constraints in the system and effects of these on diverse management styles and requirements of programs in the various NIH components. (See also response to question 4.) There seems no way to determine how to reach a single "proper balance," however, especially in view of many differing program priorities, management techniques, and other factors that each NIH component must consider in reaching decisions on most effective funding patterns to accomplish desired goals.

4. From your perspective, how effectively have NIH-supported center grants fulfilled their mission? For example, have the cancer centers with their mix of research and clinical services been successful? If so, could this approach be applied to other areas, such as neurological diseases or problems associated with aging?

Over the years a number of evaluative studies have provided sound evidence that NIH programs for center grants have been notably successful in achieving many established goals and objectives and have contributed effectively towards major advances in biomedical and behavioral research. Generally, these significant contributions have been facilitated by interactions made possible under the center grant awards. This seems to be particularly true for programs like some cancer centers, that encompass a full range of interdisciplinary R&D activities, from basic research through clinical research and community demonstrations of diagnostic, therapeutic, and preventive measures against disease. While most large NIH components award fair portions of their extramural funds for center grants, e.g., ten to fifteen percent, it is notable that two of the smaller Institutes, i.e., NIDR and NIEHS, chose to award over twenty percent of their research grant funds in Fiscal Year 1985 for centers, with a deliberate intent thusly to stimulate research interactions in their particular fields. Similarly, another Institute, NIA, has been increasing its proportion of center grants to fund, for instance, centers for Alzheimer's Disease research.

5. Is the number of basic researchers and clinician investigators in the biomedical sciences adequate to maintain the current rate of progress in the field and to meet established goals? If not, to what do you attribute this and how can it be remedied? Do you know of any quantitative data to support your views?

It seems that current numbers of basic and clinical investigators are adequate to maintain current rates of progress in the biomedical sciences. It is important at least to maintain the current level of effort. A recent study by the Institute of Medicine of the National Academy of Sciences reported, however, that current trends may presage a decline in that level, citing a recent decline in the pool of postdoctoral biomedical scientists, and pending retirements of many senior biomedical faculty members in the next few years. This suggests the possibility that greater attention will be needed soon to enhance training opportunities in the biomedical and behavioral sciences. These findings, recommendations, and corresponding data are discussed in the IOM 1985 Report, Personnel Needs and Training for Biomedical and Behavioral Research, of which I am pleased to enclose a copy.

Again, thank you for the opportunity to contribute further to the work of the Task Force. Please let me know if you wish any further inputs towards that effort.

Sincerely,

William F. Raub

William F. Raub, Ph.D.
Deputy Director for Extramural
Research and Training

Enclosure

SCIENCE POLICY TASK FORCE

Hearings on Policies for Biomedical Research

April 22, 1986

Followup Questions for Dr. Jay Moskowitz

1. **Has the traditional peer review process used by most of the biomedical research community been adequate in meeting the need for accountability of Federal funding for these programs? Can you cite specific examples? Can you suggest workable alternatives that might be considered?**

The peer review system as developed and employed by the NIH has been demonstrated to be the most effective mechanism devised to date for the effective allocation of Federal funds for the support of research and research training. Analyses of outcomes resulting from the process provide extensive evidence of its effectiveness and thus "accountability." Studies have shown that projects recommended for renewal after an initial period of support have been more productive than those that are not recommended for continuation. Bibliometric studies have demonstrated that the quality and utility of NIH-supported research far exceeds that of research that has not been supported by NIH, and several measures of career development, including publication records, rate of advancement, honors, etc., have provided unequivocal evidence of the success of the peer review system in identifying individuals who will subsequently greatly exceed the productivity of their peers.

We know of no alternative system for the distribution of research support funds that could equal the record produced by the peer review process. No other system focuses so explicitly on scientific merit or is structured in a way that reduces the opportunity for the exercise of biased perspectives to a minimum.

2. **To what extent do your evaluation projects use in-house personnel and other resources to conduct evaluations, and to what extent do you rely on external grantees and contractors? Have you found particular advantages and disadvantages to each performer for the conduct of evaluation studies?**

Current FTE limitations and long-standing departmental policy, which does not allow the use of evaluation set-aside funds to pay the salaries of Federal employees, place severe limits on the extent to which evaluation studies can be conducted with in-house personnel and resources. All major evaluation studies that have been done over the past 14 years have involved contracts. Contracts have the advantage of greatly extending the technical capabilities available in-house. However, the NIH, with its involvement in all levels of biomedical research, its intramural and extramural research and training support programs, and its extensive interactions with academia and industry as well as other Government agencies, presents to contractors great complexity and the corresponding requirement of broad knowledge and understanding of scientific and social systems. The consequence is that very high levels of professional competence with the NIH must work closely with contractors in order that all of the complexities involved in evaluation questions can be dealt with.

If larger, appropriately-trained staff were available, more evaluation studies would be conducted in-house and contracts used mainly to obtain infrequently needed technical capabilities such as computer-based data based development or survey data collection.

3. **Have you found it desirable to carry out any of your evaluation activities on a continuing basis, or are most of the projects done on a one-time basis?**

The contrast between one-time and continuing evaluation studies is comparable with the contrast between cross-sectional and longitudinal studies. They answer different kinds of questions. A decade ago, when evaluation programs were quite new, it was possible only to perform one-time, cross-sectional studies because the resources for studies over time were not available. A major focus of the development of the NIH evaluation program has been on the creation of longitudinally constructed data bases that permit us to ask questions about the long-term dynamic effects on careers and research performance of agency and departmental policies and procedures.

The ability to be responsive to the many types of questions that may be raised about NIH programs clearly requires the capacity to perform both types of studies, with decisions about the approach to be used dependent on the nature of the question(s).

4. **If NIH did not have a legislative mandate to carry out evaluations, do you think that NIH's leadership would want to continue to use a small percentage of available resources to continue to do these kinds of studies?**

In the absence of a legislative mandate, it is likely that some funds would be available to perform the highest priority analyses of readily available data about NIH programs. It is, however, due to the existence of the evaluation set-aside that NIH has the nucleus of a staff that has the requisite technical knowledge and capability to perform the studies that have been done over that past 15 years. The funds for these studies have been drawn from the individual appropriations of the NIH Institutes. As the relative ability to pay approved grant applications declines (from an average of 52 percent to 37 percent -- only 28 percent for one Institute -- during the past six years), it is unlikely that the Institute leadership will be willing to increase or even maintain the present level of contribution of funds for the purpose of conducting evaluations of policies and procedures.

When the management structure of the NIH evaluation program was changed in 1985, individual Bureaus, Institutes, and Divisions (BIDs) were required to use their own operating funds to conduct evaluations of Institute programs. In the FY 1987 Evaluation Plan just submitted to the Department, five Instuitutes proposed new evaluation studies of their programs.

5. **If you were to sum up the NIH evaluation effort over the last 15 years, what has been the most important effect these activities have had on the NIH's programs?**

The most important effect of the existence of the evaluation effort has probably been on the way program administrators approach decision-making about program development and organization. As has been pointed out many times before, the fundamental structure of NIH administrative systems is based on an evaluation construct, i.e., the peer review system. Prior to the establishment of the evaluation program, the peer review model -- i.e., the convention of groups of scientific experts in an advisory capacity -- was used almost exclusively as an aid to program policy development. Evaluation program activities have, we believe, served to infuse broad understanding, and appreciation for the need to supplement expert subjective judgment with valid objective, and preferably quantitatively based evidence. Development of the capability of producing such evidence, and demonstration of its utility through the conduct of NIH-wide studies, has been a major focus of evaluation program management in the Office of the Director, NIH.

The past decade has seen a marked increase in the employment of the products of these efforts by the NIH leadership in all types of decision-developing communication -- congressional, advisory body, professional group activity, internal program policy development and management, etc. Models developed by NIH for the assessment of science support policies have been adopted worldwide.

Mr. FUQUA. Our next witness will be Dr. Salvador Luria, Institute Professor Emeritus, Massachusetts Institute of Technology.

Mr. Luria, we are delighted you are able to join us this morning.

STATEMENT OF DR. SALVADOR LURIA, INSTITUTE PROFESSOR EMERITUS, AND FORMER DIRECTOR, CENTER FOR CANCER RESEARCH, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MA

Dr. LURIA. My name is Salvador Luria. I am Institute Professor Emeritus at MIT. Until my retirement last year, I was director of the MIT Center for Cancer Research. I am currently senior scientific advisor at Repligen, a private biotechnology corporation.

It is a privilege to appear before this committee, whose oversight of many agencies active in biomedical research has contributed to making, in my opinion, the House of Representatives the most supportive proponent of biomedical research in the United States.

The record of American biomedical research speaks for itself. All nations look with admiration and envy at the research structure we have built in this area. All people, and maximally the American people, benefit from its impact on human health and on the quality of life. At the center of the U.S. effort in biomedical science are the National Institutes of Health. Working hand-in-hand with the National Science Foundation at the interface between biology and medicine, NIH has established a unique record of in-house and extramural research effectiveness, and it has contributed to maintaining the highest standards of research quality and the prompt transfer of knowledge from the basic to the applied fields.

I look upon the past 10 years of biomedical research as a period of unprecedented progress. Ten years ago, for example, we talked of immunology in terms of antibodies and vaccines empirically derived from medical practice. Today we know precisely how the human body generates, out of a few well-identified genes in its cell chromosomes, the millions of different defense mechanisms against foreign intruders and toxic substances. Today we can prepare monoclonal antibodies—that is, antibodies in which each molecule is directed against the same chemical portion of a toxin or a virus—against each portion of a toxin or a virus, and we are on the way to using them to combat cancer cells. In the cancer field, 10 years ago we were struggling to understand what happens when a cell becomes malignant. We have fought cancer as best as we could, with some success, with therapies whose basis was poorly understood. Today, side-by-side with the progress in chemotherapy fostered by the brilliant leadership of the National Cancer Institute, we have gained a profound understanding of cell malignancy. We have discovered and isolated oncogenes–the first time in our own Center for Cancer Research by Professor Weinberg. A change of structure or control transforms a normal gene into a gene for malignancy. Many oncogenes have been extracted, shown to transmit malignant properties to normal cells and their products have been identified. I predict that in 10 years the central theme of cancer therapy will be directed to inhibiting or destroying these oncogene products.

These and other advances have resulted from the growth of a new branch of life science, molecular biology—a merger of genetics and biochemistry—and of its direct offspring, genetic technology. These are based on the newly acquired capacity to isolate and analyze the DNA of individual genes and the protein products at the molecular and atomic level. This has given biomedical scientists a deeper understanding of processes like cancer. Now we must learn how to inhibit or destroy specifically the products of the cancer genes within the cells. If I may use a far-fetched comparison, in cancer research 10 years ago we were like a garage mechanic trying to fix a car engine without knowing how the engine worked. Today, we are rather like a mechanic who knows all about engines but still has to find the key to the car. I believe the key to the cancer problem is forthcoming.

Now let me mention AIDS, the most recent scourge. The speed with which research on AIDS has progressed, mainly at the NIH but also in other centers of research here and abroad, is little short of amazing. The virus has been isolated, each of its genes separated and identified, and their products have been recognized. Research has generated tests of AIDS infection and the road to an effective vaccine is now open, subject to careful and successful testing. Most of this achievement comes from knowledge and technology that were unknown 10 years ago. It is remarkable that so much progress has actually stemmed from in-house research at NIH, including the most recent report, a couple of weeks ago, of the isolation of a most promising vaccine against AIDS with the virus, or the antigens in virus genes introduced into the vaccinia virus, which we know can be tolerated.

While promoting nationwide biomedical research, the NIH has operated what I call without hesitation the most powerful single biomedical research institution in the world today. The reason for the success of NIH programs, both intramural and extramural, in medical schools and universities has, in my opinion, been due to the rigorous machinery developed by NIH for quality control and priority choice, as well as by the positive financial support by the Congress. The NIH operation has succeeded because it has resisted fads and has pursued excellence. At every level, from the National Advisory Council to each of the Boards and Study Sections, a sound machinery, effective peer review, has been generated and maintained. In the 1984 report of this committee, on page 50, of this task force, the question was raised of selection procedures alternative to peer review. I am 100 percent for peer review as it exists today at NIH. Complaints registered in certain quarters reflect not any unfairness of the system, but the pressures on selection among research proposals at times of limited funding.

There is nothing more disheartening and upsetting to the pursuit of science than the annual threat of overall cuts in financial support. Certainty of continuing support on a reasonably long term, at least several years, is essential to prevent the waste of time devoted to prepare new applications and the uncertainty in planning long-term research programs. More important, guarantee of funds for a few years encourages young investigators into embarking into the fascinating but arduous pursuit of biomedical science without fear of being at the mercy of some arbitrary change in economic policy.

The organization of scientific research achieved by NIH may well serve as a model also for other agencies whose mandate is more narrowly focused. It is my understanding, and I made some inquiries in the past 2 weeks spurred by the request that is defined today, that the research effort of the Veterans' Administration is modeled in many aspects on that of NIH and has been, within its specified domain, quite successful. Research quality has been excellent and competently carried out, while remaining targeted on the areas of medicine of concern to veterans and their environment. The question of centralized quality control may deserve some attention. Continuity of research support from year-to-year is actually more secure at the VA than for extramural NIH research.

The third agency under the supervision of the committee is the Food and Drug Administration. FDA is a regulatory agency and the research it sponsors must, presumably, be of a more practical nature than, for example, that of NIH. Research by FDA is less visible and harder to evaluate, and may vary in depth or conclusiveness. Like all regulatory agencies, FDA is currently caught in the tension between the public demand for effective watch-dog function and the philosophy of the present Administration to minimize regulation of the private sector. Perhaps a more formal approach to regulatory agencies such as an advisory research council comparable to that of NIH and VA could help.

In the case of genetic engineering, the NIH was given, in 1974, unusual regulatory supervision. It has performed it well, generating a set of explicit guidelines that could be revised whenever experiences required it by a high-level board. It was a remarkable achievement in regulation, a practice that made possible the safe development of a new science and also of a new industry.

Finally, I wish to express my concern about a recent increase of involvement of the military into biomedical research. The Office of Naval Research and DARPA have recently initiated a large program of graduate student support in the specific area of biotechnology. My concern is not so much that the moneys thus entering universities will convert biomedical research to military purposes, such as biological warfare, which has been prohibited by Congress; rather, I see the danger that targeting enormous sums of money to support research training in one specific area will distort the balance of research in different fields, weaken biomedical science, and turn a generation of students into narrow technologists, rather than broadly trained scientists.

Thank you.

[The prepared statement of Dr. Luria follows:]

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DISCUSSION

Mr. **Fuqua**. Thank you very much, Dr. Luria.

In your broad area of background and experience in biotechnology and having been a recipient of a Nobel Prize, what has been probably the most productive area of biotechnology research in the last 20 years?

Dr. **Luria**. Specifically, Mr. Chairman, you refer to biotechnology or——

Mr. **Fuqua**. Biomedical research.

Dr. **Luria**. Or biomedical research?

Mr. **Fuqua**. Yes.

Dr. **Luria**. I would say that in terms of research the advances that have been made has come from the joining of fields. The most important thing has been the joining of the fields of cancer research, immunology and human genetics.

Mr. **Fuqua**. Multidisciplinary?

Dr. **Luria**. Interdisciplinary area. This is really where NIH and NSF have been very important: NSF from the point of view of basic biological science; and NIH bringing in the needs and the experience from the medical field.

Mr. **Fuqua**. Do you think trying to zero in, as Congress has focused on through areas like the NIH, on health problems such as cancer, heart disease, neurological disease lends itself to a faster solution to those problems, or would that have happened anyhow?

Dr. **Luria**. Let me take an example with which I have had some experience, which is the National Cancer Program, which started in 1971. I was one of those who were involved from the very beginning in planning it in such a way to see that it did not become detached from the other areas of biomedical science. I think that despite the fact that there have been criticisms and questions about the matter of how separate funding would affect these things, I believe that the overall result has been very impressive.

I think that it has certainly been impressive, if nothing else, from the point of view of sense of safety, to have an institution that has both promoted as fast and, as well as possible, the approach directed to the therapy of cancer, even using semi-empirical methods, like much of chemotherapy had to be, and at the same time has pushed basic research to the point that now, today, we have at least 40 single oncogenes extracted from human cancers, each of which can be extracted and proved, if placed in human cells in culture, to produce again cancer cells. And what now we have to do is to bring the therapy and the research together into a more powerful system.

The progress of immunology has been tremendous in these years. I take some pride that Dr. Tony Gower, who broke the key to the secret of how the variety of immunity mechanisms have been generated is now—I brought him to the MIT Center for Cancer Research where he is now working. The convergence represented by the fact of such people brought together into institutions supported by the NIH without depriving other people of the necessary support seems to me a tremendous sense of effectiveness. I wish every other agency of the Government could match what the Health and Human Services Department has done in this area.

Mr. **Fuqua**. How would you go about advising us on a balance between directed research and nondirected research, and who should be making those decisions? Could all of it be in directed research, or should there be a balance between directed research and nondirected?

Dr. **Luria**. Mr. Chairman, I think I understand correctly. When I say directed, it means targeted.

Mr. **Fuqua**. Yes.

Dr. **Luria**. Because I think, as I heard Mr. Walgren asking questions before, that is a very important point that you made; about how the wisdom of the NIH Council is used in order to balance. If you are now asking about the targeting in various Institutes within the Institutes of Health, I believe that that, in a sense, results almost automatically from the quality control that is exerted within the Council in this following sense. If there is an area of science in which, let's say, the advances are rapid, it is because that is an area of science with increased possiblity of advances, and that will be sustained. If there is some area of science in which progress has been low, very seldom this has been slow because it has not been supported or encouraged; it has been slow because one cannot do it.

Peter Medawar, the famous, great scientist and science writer from England, has defined science as the art of the possible, and this is something one has to remember. You can give me a billion dollars to find a treatment for a disease for which I don't know the mechanism, I would not know how to do it. On the other hand, let me give you a little example of how well applied things works.

A person I know well, a scientist at the Harvard School of Public Health who was a student at MIT and then at Harvard in genetic engineering, had the idea of comparing fragments of the DNA from a whole variety of pathogenic leishmaniasis. It is one of the agents for one of the most widespread and terrible diseases in Africa and in parts of Asia, and also in South America. And by this genetic test, it is now possible, because of the work of Dr. Diane Wirz, to take an epidemiological study and find out right away which ones of those are infected with the severe potentially killing form of this disease, and therefore have to be treated immediately, although the treatment is very painful, and the ones which are infected with the disease which is likely to give two weeks symptoms and disappear. Until the technique was available, we, of course, tried to diagnose leishmaniosis as severe or nonsevere, but there was no way of doing it. You will have to understand it.

Mr. **Fuqua**. Mr. Walgren.

Mr. **Walgren**. Thank you, Mr. Chairman.

What should be our response to the thought that, with respect to cancer research, there are lots of scientifically sound research proposals that are not funded? We, of course, wish they were. But is that because we are failing to push enough money into that? And if it is because we are not pushing enough money into that, how do you distinguish between our failure to push money into that, and a similar failure to push money into arthritis, or push money into diabetes, or push money into any particular target that always gets knocked down as the disease of the month? If we should push money into cancer, isn't the obligation the same to push money into the others? And if that is true, then it would seem that we are the ones that have to decide how much effort to put into these areas and we cannot give over that responsibility to any other range of administrative decisionmaking.

Dr. **Luria**. Well, I think that is a very important problem. The biomedical research field has grown in all directions because of the availability of new power to solve problems. There is no question. Twenty years ago most of the things one can do now, and most of the things on which the proposals are based, did not exist, or were not even conceivable sometimes. So the question is with these enormous increasing possibilities it has been, I believe, the responsibility of people like myself who have sat in Study Sections, the responsibility of Advisory Councils like those of the NIH or other agencies to slice the pie according to the wisdom that was available to them. If there is a certain sum X available and if the certain sum X is to be distributed among the various branches of research, it means simply that probably in branches of research in which progress is a little bit less rapid, or quite a bit less rapid you have to be a little bit more strict in your evaluation. And you are going to get, for example, the people necessarily are going to vote a little bit lower certain proposals because there is a certain number or limit of proposals that can be funded.

I think that this is where—I was delighted to hear your question, Mr. Walgren, about how the Councils function. I think that the Congress should really see very closely what it is that the organization for biomedical research has accomplished. I think it is a uniquely effective thing. I hate to make comparisons, but I believe that that kind of organization, if it were in the Department of Defense, we would all be feeling much safer today than we are.

I believe that the wisdom that has been brought by a succession of, not so much of directors, but the members of the Advisory Council taken from every branch has been very remarkable. All I can say is that we have struck a balance. I have mostly been involved in matters of either cancer research or microbiology, which was my original field. I don't know very well how it works for other scientists, although, in fact, for many years because of the arthritis and infectious diseases I have received support for my own research from that Institute.

Well, I believe that altogether there is no segment of the NIH of which we can say that it has gone wrong. Some of them may have been starved, only in the sense everybody has been starved in the last 2 years.

Let me say one thing. All of the information I have gotten in my inquiries pointed out the importance of the collaboration between agencies. For example, in many cases the Veterans' Administration has made it possible for certain important projects to be carried out when moneys were not available or sufficient within NIH, and that is a very important aspect of what I call the overall organization of American biomedical science.

Mr. **Walgren**. You mentioned that in setting up the cancer entity you tried to keep it related to a wider range—well, I don't know. You said you tried to keep it related to the other disciplines or the other efforts going on at NIH and not——

Dr. **Luria**. Competed.

Mr. **Walgren** [continuing]. Not competitive. I guess what I wanted to ask was can you describe the concept of separateness and yet the concept of related to? Because that is an area that apparently has worked quite well.

We in the Congress, as I gather, focused on cancer and said we want this area developed apparently to the exclusion of others, I gather. At least the money was targeted. And yet, apparently it was targeted, but kept related, or kept not separate. Can you describe that a little bit more fully?

Dr. **Luria**. I was only a participant, Mr. Walgren. I was not in any authority position. In 1971, when the idea of the national cancer attack plan was developed, several hundred scientists were brought together for several repeated 2-day sessions in which we not only analyzed and broke up the approach to cancer research and cancer treatment, and so forth, into various sectors, but also discussed the question of how this could work and get the maximum support for the cancer research without interfering or destroying some other branches. And that certainly is what has happened. I think it has happened I would say, not especially for the wisdom that was exerted at that time, but because of the fact that cancer research merged with the fundamental biological research by its own impetus, by its own momentum.

And I think—let me say, for example, even taking the most extreme kind of things like when I was one of the first people to do biological research on viruses other than medical. And in the 1940's, Delbruck, Hershey, and myself did the first work on the biology of certain viruses. One of my students, and also a recipient of a Nobel Prize, Dr. Renato Dulbecco, was the first one who developed the study of single genes of a virus as a possible agent to transforming cancer. And you will hear I think more from Dr. Temin, if he is not too shy about his own achievements, about some of the other things.

The fact is that all of this just came together in the structure of biology. I think the most important thing that has happened, and I believe it was done very well, is for the various Institutes of Health and the National Cancer Center to work hand-in-hand, rather than in competition. I have a great admiration for Dr. DeVita, who has been able to live in the Center with an extremely complex kind of situation with the Presidential committee, a board of his own, and the NIH, and so on. And it has been a very fruitful leadership. I think we can do it. When the Congress gives us the means without flooding them suddenly with the order to do something about washerwoman, or something about ingrown toenails—we cannot do anything about ingrown toenails. We can study the structure of the skin and then, once we know more maybe we can do it.

Mr. **Walgren**. Can you define the symptoms of flooding something with money? Are there things that immediately crop up? You mentioned the distorting of the scientists into narrow technologies. Are there other signs that we should be sensitive to if an area is getting too much support?

Dr. **Luria**. I believe that is a very important thing. I think that it would be extremely dangerous, taking the same example I used here, it would be extremely dangerous if the Congress were to say, well, ONR and DARPA are putting $1,800 million in biotechnology training, so we don't have to do it, or we don't have to push for maintaining. I think frankly that that is a danger. The danger is because instead of being in the hands that have directed until now the direction is going to be skewed. This is what I mentioned.

If you are asking more specifically, I would say that the Congress has it seems to me a—I shouldn't say the word responsibility—but the Congress has an opportunity to find out from the public what is on their mind and to inquire whether the research establishment is aware of that, and then create a communication between the different agencies, and so on, if it does not already exist.

I think we don't have any way of finding cut. All the newspapers give us is three-times-filtered information. But you can get the information because you are their representatives. That is what we need.

Mr. WALGREN. An interesting point. Yes. I think that is a real interesting point.

Let me ask one other question, if I might, Mr. Chairman.

What is your greatest frustration other than the difficulties of the science?

Dr. LURIA. Seventy-three and a half years of age. At the moment. [Laughter.]

Mr. WALGREN. OK. Thank you, Mr. Chairman.

Mr. FUQUA. Thank you very much, Dr. Luria.

Dr. LURIA. Thank you, Mr. Chairman.

Mr. FUQUA. We appreciate your contributions here this morning.

[Questions and answers for the record follow:]

SCIENCE POLICY TASK FORCE

Hearings on Policies for Biomedical Research

April 22, 1986

Followup Questions for Dr. Salvador E. Luria

1. **As you look back over the last 10-20 years, how would you view the relative success of biomedical research programs in the different Federal agencies from the standpoint of contribuitng information to the national science base? To technological innovation? To benefit the public health? Do you see a need for any modifications in the programs, policies, or practices? Or in Government support? If so, how could this be achieved?**

   The records of NIH (including NCI) and NSF have been excellent despite lack of substantial increases of funds and despite the "emergency" atmosphere created by short-range financing of projects. The response to the AIDS crisis has been good despite equivocation at the top Executive level. Programs should include longer range grants with biennial reports.

2. **From your background and experience, is there a basic difference between research in the physical sciences and in the biological sciences? Is the research strategy different because of the nature of the research? Can certain strategy models which are successful in one be applicable to another? Will the research strategies in biomedical research change to reflect the interdisciplinary nature of many of the current projects? In the short-term? In the long-term?**

   Strategy in physical science, before nuclear power and weaponry, was dictated by uniformity of problems and reproducibility of measurements done anywhere. After 1945, physics became megaphysics, which is technology applied to very large problems. Biology proceeds by attacks in many scattered problems of interest, with occasional convergence. Technology has provided enormous services without creating megabiology.

3. **From your extensive background and experience in biomedical research, how has the field changed over the last 20 years? Is it more costly to do research as our information base has increased and techniques have become more quantitative and refined? How will fluctuations in Federal funding affect progress and will productivity be jeopardized in times of fiscal constraint? Can the private sector fill the void in these cases?**

   Technological advances have not in-and-by themselves increased costs of biological research, but have made possible for more researchers to be productive, and therefore have increased the total need for financial support. Steadily rising support without significant fluctations is important to allow the scientific enterprise to remain attractive to science-oriented young people and to stabilize careers in biomedical science. The private sector can hardly replace or meaningfully supplement Government support beyond providing some fellowships and (pointless) prizes.

4. **In terms of the role of Congress in setting funding priorities and levels in biomedical research and health policy, how can the present process be better informed and improved?**

Whatever its supposed shortcomings and fallacies, the current peer review system has been successful. It has not yielded to the "baronal" system that affects certain European review systems. The peer review through study sections can be improved by careful selection of participants on the basis of their personal competence and maturity as well as of their areas of research experience.

5. **As you look ahead to the year 2000, what areas of biomedical research do you see as the most promising? Is it possible to make predictions of this kind, recognizing that the chance finding also leads to fruitful research areas? How would you advise a young investigator "just starting out" as to which research field to enter?**

I don't like predictions, but I am willing to advise young investigators just starting out to keep sufficiently close to the mainstream of molecular and cellular biology because of the power intrinsic in these approaches. Cancer research at these levels should be productive not only in relation to cancer but also human development.

Mr. **Fuqua**. We do have a time problem. We are going to have to move on to Dr. Howard Temin, McArdle Laboratory for Cancer Research. We do have another meeting in here in 25 minutes, so we will have to move along before we get evicted from the room.

Mr. Temin, we are very pleased to have you this morning.

STATEMENT OF DR. HOWARD M. TEMIN, PROFESSOR OF ONCOLOGY, MCARDLE LABORATORY, UNIVERSITY OF WISCONSIN-MADISON, MADISON, WI

Dr. **Temin**. Thank you. I will try and go quickly, since Dr. Luria touched on some of the points I will make. I guess I should also say that I am a scientific grandchild of Dr. Luria, since I got my degree with Dr. Dulbecco, who he mentioned as one of his students.

Mr. **Fuqua**. And also a Nobel Prize winner.

Dr. **Temin**. Yes. So I will just skip ahead since you know who I am.

Federal Government support of biomedical science is one of the great success stories of the last decades in the United States. Our system of research in university, Government, industrial, and independent laboratories with Government, voluntary, and industrial support is the best in the world and envied elsewhere. Federal support of biomedical science is one of the few areas of Federal involvement where there is general satisfaction with the system and its products.

To illustrate this, I will discuss my own career and also talk about the response of the biomedical research community to the AIDS epidemic.

I started in biomedical research 30 years ago as a graduate student at the California Institute of Technology. At that time molecular biology was just beginning and the molecular study of animal viruses did not exist. We knew little about animal viruses. We could see them in the electron microscope and we could study them using indirect methods, but it was hard to make definite statements about how viruses replicated.

In 1960, I moved to the University of Wisconsin, a major State research university, and I applied for my first research grant. It was rejected by the virology study section on the grounds that I was too young. Fortunately, the governing council that you have heard about earlier today had a member from the University of Wisconsin who prevailed upon the council to award me the grant. Now there is more awareness of the need to support starting young investigators, and there are many mechanisms to help them begin independent laboratories.

My work was very unorthodox, but my grants were still fully supported by the NIH because the experiments I proposed were reasonable and tested my unorthodox hypothesis.

However, not every unorthodox idea is worth supporting. For example, I have been told that one scientist, worried about a perceived failure of journals to publish really original research and ideas, founded a journal that would publish all submitted papers. Soon he found that many of the papers he received had such wild, but original ideas that he had to institute some selection in review process.

It is very easy to ask general questions in biology. What is hard is to pose questions that are important and testable. Every scientist wants to be original in that way. To illustrate this point further, in 1970, I proposed that certain kinds of viruses and certain kinds of cellular genes were evolutionarily related. This idea was original, but it was essentially ignored for 10 years because it was not testable. Now, because the methodology is available, it has been tested and shown to be correct and is now generally accepted.

This story illustrates how our knowledge and our abilities to get answers in biomedical science have grown, primarily as a result of Federal support. For example, our knowledge of animal viruses has enormously increased. Furthermore, the speed of acquisition of knowledge and the detail and concreteness of our knowledge are enormously greater.

I shall illustrate with two examples: the relationship of oncogenes and growth factors, and AIDS. Twenty years ago I proposed that specific genes in tumor viruses increased the utilization of growth promoting factors in serum. Not too much could be done to test this hypothesis then, and, in fact, I stopped working on it in the early 1970's. However, now through the work of numerous others, primarily supported by Federal funds, we know that there are a series of specific normal genes coding for specific protein growth factors, receptors, modifiers, and enzymes, that can be mutated to form cancer genes or oncogenes. This knowledge helps in defining the nature of cancers and suggests methods for treatment and prevention.

Another example. In the late 1970's and early 1980's, astute clinicians in several places in this country noted an unusual combination of rare diseases and recognized a new disease: AIDS [acquired immune deficiency syndrome]. Within 2 or 3 years of the recognition of this disease, biomedical scientists had isolated the virus causing the disease, discovered its mode of transmission, and instituted tests and other measures to control the spread of the epidemic. Similarly, when Legionnaire's disease and toxic shock syndrome appeared, control measures were soon forthcoming.

How did this happen? Research, primarily supported by the Federal Government, had over the past two decades provided a base of knowledge, techniques, and laboratories that could analyze AIDS and its cause. Unfortunately, we still have more to do.

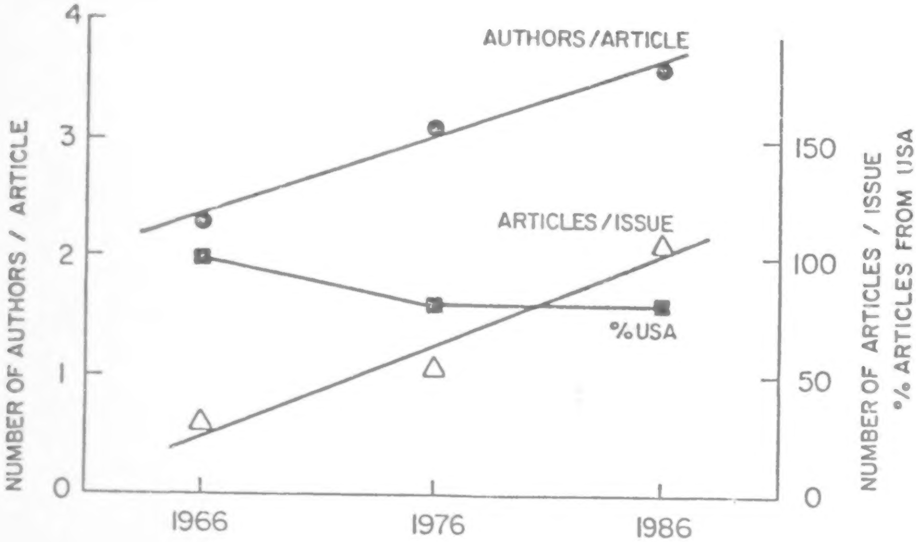
What are the features of the Federal support of biomedical research that led to such an impressive response? The support had been continuous, consistent, and predictable; had involved a multiplicity of types of institutions and of investigators; had provided for training of new investigators; and had not insisted upon a narrow and immediate disease orientation. Thus, the knowledge base was not developed for AIDS, but it did provide a background for understanding and controlling AIDS.

The effectiveness of the response to AIDS benefited from the close coupling of basic and applied research as illustrated, for example, by research on certain chicken and cat viruses being immediately relevant to human AIDS. The close coupling of biomedical research to public health measures and the need for both is also shown by the AIDS epidemic. Basic research provided the knowledge base and testing tools to carry out public health measures.

The problems of intravenous drug users infected with AIDS virus also illustrates the need for both curative and biological and behavioral preventive approaches to controlling this epidemic. The close connection of all biomedical research is also shown by the fact that it was scientists interested in cancer who made the background discoveries which were crucial to understanding AIDS, an infectious disease.

It should be emphasized that this knowledge base provides a basis for understanding any other new diseases and other medical problems such as genetic diseases and aging.

However, in the last two decades, as indicated in the accompanying figure, there have been large changes in the structure of biomedical science in the United States. There are more investigators, there are more investigators working cooperatively on problems because of the numerous techniques required—those are the two curves going up—and there are more foreign scientists doing equivalent work—and that is the curve going down, percent of the U.S. scientists. In terms of AIDS, for example, French scientists did some of the pioneering virus work. These structural changes are also important in the biotechnology industry where the U.S. predominance is threatened.



JANUARY ISSUES OF P.N.A.S., U.S.A.

These structural changes and the squeeze on Federal funding have raised problems and highlighted disturbing tendencies in U.S. Government support of biomedical research. Instead of trying to nurture and maintain this structure and the personnel in biomedical research that have served the country so well, we see the beginning of a falloff of support for biomedical research. Money for grants and money to train new investigators is not increasing and may be cut. This is ironic in light of the increased need for several approaches to problems, the increased number of people, and the great opportunities. Will we be ready so successfully when the next AIDS epidemic appears?

Incomprehensible to many scientists is the disproportion between moneys spent to defend against perceived external enemies and moneys spent to defend against the more immediately dangerous internal viral and metabolic enemies, like the AIDS virus and high cholesterol, which rob us of health and life.

We scientists perceive in the Federal Government a lack of long-range planning or of consideration of long-range effects in maintaining the strength and continuity of the biomedical research community. We feel there is little understanding of the detrimental, long-term effects of the lack of consistent, continuous, and predictable support upon the people and institutions that carry out biomedical research. There is concern that the peer review system based upon merit is being discarded in favor of nonscientific, political criteria. One current example is the special bills to support construction at particular institutions without prior peer review. There is concern about lack of understanding that the difference between direct and indirect costs is bookkeeping and that both are real costs of research. Direct costs are individually billed costs; indirect costs are aggregated costs. We feel there is little appreciation of the effect on costs and on time of the numerous and increasing bureaucratic requirements faced by an active biomedical researcher supported by Federal funds.

What of the future? This depends very much upon what you in the Congress do. You can maintain and strengthen the biomedical research system or you can be responsible for its decline. We now have a system that works and works well, as illustrated by the response to AIDS and by the discovery of the role of oncogenes in cancer and normal cell growth. These are but a few of numerous other examples that could be mentioned. The only major problem is the limited funding, and it is not realistic to expect industry or voluntary organizations to replace Federal funds. They can only supplement them.

I can make some suggestions for small changes in the system that might be useful, but primarily I ask for continued backing of what has been a successful system. In particular, I ask for steady long-term support for 6,000 to 7,000 new and competing NIH and ADAMHA research grants a year.

Other recommendations. When research funds are inadequate to fund all meritorious grants as at present, it is inevitable that some good investigators have periods with no research support. Therefore, some system to maintain investigators and their laboratories at a minimal level for a year or two until they can get replacement funding is necessary to permit their laboratories to function in the interim. Many people believe that paying some grants at less than full amounts to increase the number of investigators who have a funded grant is one way of meeting this problem.

Since it has been concluded by Government bodies that 10 years of graduate and postdoctoral training and experience are needed to prepare an independent investigator, it is essential that we preserve a system that keeps the pipeline full. Otherwise, in 10 years time we may find that we do not have the young investigators to meet the next AIDS epidemic.

Our concern is that with the reduced funding younger people will not enter biomedical research. Moreover, some present investigators will switch to other fields or to profitmaking institutions rather than continue in basic biomedical research. If that happens, we will be unable to exploit fully the opportunities present to us today and respond fully to the medical problems today and in the future.

Thank you. I shall be pleased to answer any questions.

[The prepared statement of Dr. Temin follows:]

Testimony of Howard M. Temin

McArdle Laboratory
450 N. Randall Ave.
University of Wisconsin
Madison, Wisconsin 53706

before House Committee on Science and Technology

Task Force on Science Policy

Hearing on Policies for Biomedical Research

April 22, 1986

I am pleased to be able to appear before this Task Force to give my impressions of the present status and future effects of Federal Government involvement in biomedical research. Later I shall be pleased to answer your questions. I am Howard M. Temin, Professor of Oncology at the University of Wisconsin-Madison. I was awarded the Nobel Prize in 1975 for research on how viruses cause cancer. For the last thirty years, I and my laboratory have been primarily supported by US government funds, although my salary now is paid by the American Cancer Society and the University of Wisconsin. Thus, it might appear that my testimony is self-serving and prejudiced. However, I believe that as a professional research scientist my training enables me to speak fairly about matters in which I have such a personal involvement.

Federal Government support of biomedical science is one of the great success stories of the last decades in the United States. Our system of research in university, government, indusurial, and independent laboratories with government, voluntary, and industrial support is the best in the world and envied elsewhere. Federal support of biomedical science is one of the few areas of Federal involvement where there is general satisfaction with the system and its products.

To illustrate why I believe that Federal support of biomedical research has been generally satisfactory, I'll discuss my own career and also talk about the response of the biomedical research community to the AIDS epidemic.

I started in biomedical research thirty years ago as a graduate student at the California Institute of Technology. At that time molecular biology was just beginning and the molecular study of animal viruses did not exist. We knew little about animal viruses. We could see the viruses in the electron microscope, and we could study them using indirect methods, but it was hard to make definite statements about how viruses replicated.

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It is very easy to ask general questions in biology. What is hard is to pose questions that are important and testable. Every scientist wants to be original in that way. To illustrate this point further, in 1970 I proposed that certain kinds of viruses and certain kinds of cellular genes were evolutionarily related. This idea was original, but it was essentially ignored for ten years because it was not easily testable. Now, because the methodology is available, it has been tested, shown to be correct, and is now generally accepted.

This story illustrates how our knowledge and our abilities to get answers in biomedical science have grown, primarily as a result of federal support. For example, our knowledge of animal viruses has enormously increased. Furthermore, the speed of acquisition of knowledge and the detail and concreteness of our knowledge are enormously greater.

I shall illustrate with two examples - the relationship of oncogenes and growth factors and AIDS. Twenty years ago I proposed that specific genes in tumor viruses increased the utilization of growth promoting factors in serum. Not too much could be done to test this hypothesis then, and in fact I stopped working on it in the early 1970s. However, now through the work of numerous others, primarily supported by federal funds, we know that there are a series of specific normal genes coding for specific protein growth factors, receptors, modifiers, and enzymes, that can be mutated to form cancer genes or oncogenes. This knowledge helps in defining the nature of cancers and suggests methods for treatment and prevention.

Another example: in the late 1970's and early 1980s astute clinicians in several places in this country noted an unusual combination of rare diseases and recognized a new disease - AIDS, acquired immunodeficiency syndrome. Within two or three years of the recognition of this disease biomedical scientists had isolated the virus causing the disease, discovered its mode of transmission, and instituted tests and other measures to control the spread of the epidemic. Similarly when Legionnaire's Disease and toxic shock syndrome appeared, control measures were soon forthcoming.

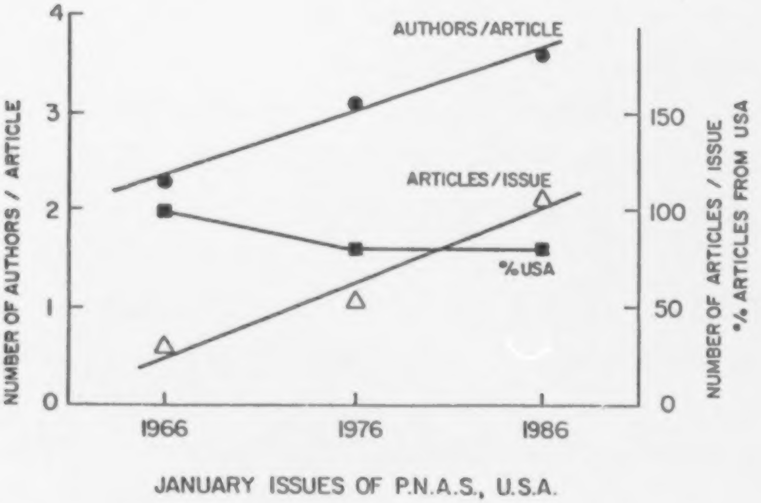
How did this happen? Research, primarily supported by the Federal Government, had over the past two decades provided a base of knowledge, techniques, and laboratories that could analyze AIDS and its cause. (Unfortunately, we still have more to do. We do not have ways of preventing the AIDS virus infection except by avoidance, and we lack good treatments for the infection and disease.)

What are the features of the Federal support of biomedical research that led to such an impressive response? The support had been **continuous, consistent**, and **predictable**, had involved a multiplicity of types of institutions and of investigators, had provided for training of new investigators, and had not insisted upon a narrow and immediate disease orientation. Thus, the knowledge base was not developed for AIDS, but did provide a background for understanding AIDS.

The effectiveness of the response to AIDS benefited from the close coupling of basic and applied research as illustrated, for example, by research on certain chicken and cat viruses being immediately relevant to human AIDS. The close coupling of biomedical research to public health measures and the need for both is also shown by the AIDS epidemic. Basic research provided the knowledge base and testing tools to carry out public health measures. The problems of intravenous drug users infected with AIDS virus also illustrates the need for both curative and biological and behavioral preventive approaches to controlling this epidemic. The close connection of all biomedical research is also shown by the fact that it was scientists interested in cancer who made the background discoveries which were crucial to understanding AIDS, an infectious disease.

It should be emphasized that this knowledge base provides a basis for understanding any other new diseases and other medical problems such as genetic diseases and aging.

However, in the last two decades, as indicated on the accompanying Figure, there have been large changes in the structure of biomedical science in the US. There are more investigators, there are more investigators working cooperatively on problems because of the numerous techniques required, and there are more foreign scientists doing equivalent work. (In terms of AIDS, for example, French scientists did some of the pioneering virus work.) These structural changes are also important in the biotechnology industry where the US predominance is threatened.



These structural changes and the squeeze on Federal funding have raised problems and highlighted disturbing tendencies in US government support of biomedical research. Instead of trying to nurture and maintain this structure and the personnel in biomedical research that have served the country so well, we see the beginning of a fall off of support for biomedical research. Money for grants and money to train new investigators is not increasing and may be cut. This is ironic in light of the increased need for several approaches to problems, the increased number of people, and the great opportunities. Will we be ready so successfully when the next AIDS epidemic appears?

Incomprehensible to many scientists is the disproportion between moneys spent to defend against perceived external national enemies and moneys spent to defend against the more immediately dangerous internal viral and metabolic enemies, like the AIDS virus and high cholesterol, which rob us of health and life.

We scientists perceive in the Federal Government a lack of long-range planning or of consideration of long-range effects in maintaining the strength and continuity of the biomedical research community. We feel there is little understanding of the detrimental long term effects of the lack of **consistent**, **continuous**, and **predictable** support upon the people and institutions that carry out biomedical research. There is concern that the peer review system based upon merit is being discarded in favor of non-scientific, political criteria. One current example is the special bills to support construction at particular institutions without prior peer review. There is concern about lack of understanding that the difference between direct and indirect costs is bookkeeping and that both are real costs of research. Direct costs are individually billed costs; indirect costs are aggregated costs. We feel that there is little appreciation of the effect on costs and on time of the numerous and increasing bureaucratic requirements faced by an active biomedical researcher supported by Federal funds.

What of the future? This depends very much upon what you in the Congress do. You can maintain and strengthen the biomedical research system or you can be responsible for its decline. We now have a system that works and works well as illustrated by the response to AIDS and by the discovery of the role of oncogenes in cancer and normal cell growth. These are but a few of numerous other examples I could mention. The only major problem is the limited funding. (It is not realistic to expect industry or voluntary organizations to replace federal funds.)

I can make some suggestions for small changes in the system that might be useful, but primarily I ask for continued backing of what has been a successful system. In particular, I ask for steady long term support for six to seven thousand new and competing NIH and ADAMHA research grants a year.

Other recommendations: when research funds are inadequate to fund all meritorious grants as at present, it is inevitable that some good investigators have periods with no research support. Therefore, some system to maintain investigators and their laboratories at a minimal level for a year or two until they can get replacement funding is necessary to permit their laboratories to function in the interim. Many people believe that paying some grants at less than full amounts to increase the number of investigators who have a funded grant is one way of meeting this problem.

Since the Institute of Medicine Committee on National Needs of Biomedical and Behavioral Research Personnel concludes that 10 years of graduate and post-doctoral training and experience are needed to prepare an independent investigator, it is essential that we preserve a system that will keep the pipeline full. Otherwise, in 10 years time we may find that we do not have the young investigators to meet the next AIDS epidemic.

Our concern is that with the reduced funding younger people will not enter biomedical research. Moreover, some present investigators will switch to other fields or to profit making institutions rather than continue in basic biomedical research. If that happens we will be unable to exploit fully the opportunities present to us today and respond fully to the medical problems today and in the future.

I shall be pleased to answer any questions.

DISCUSSION

Mr. **Fuqua**. Thank you very much, Dr. Temin.

From your perspective as a very distinguished researcher, is it possible to determine which projects may yield results that would probably lead to successful clinical applications?

Dr. **Temin**. The only criteria that can be used about determining which projects will yield results is to make sure that they are sound scientific proposals. No matter how much money is spent, if a proposal is not scientifically sound, there will be no worthwhile results from it. It is important only to fund works that are of scientific merit. They will give useful results.

Now which ones will lead to successful clinical applications? We can only tell that in the future. For example, the work that led to the applications in AIDS, of tests for the virus, were developed for completely different things that had nothing to do with AIDS, nothing to do with human diseases. It is very difficult beyond a very short period of time to tell what is going to lead to the most useful clinical applications.

Because all biological systems are related, work that appears to be untargeted and unrelated will, in 10 years time, turn out to be directly applicable to a disease. So we can only target directly for a very short period of time. Beyond that we cannot.

Mr. **Fuqua**. How would you—I asked this question earlier and possibly you were here then. How do you develop a balance between targeted or directed support and those nontargeted or nondirected supports?

Dr. **Temin**. I think it is important to realize and to accept that there is a difference between the words and what is actually carried out. I think it is completely appropriate to target things at your broad level, and I hope that you continue to do so. I think it is also appropriate and very necessary that you let us decide how to carry out the targeting. Is it clear what I am saying?

Mr. **Fuqua**. Yes.

Dr. **Temin**. In other words, when the war on cancer came or now, if there will be an increase in funding for AIDS, we will accept that that is the goal. But it is very important to let us, meaning the people who are carrying out the work and understand the nature of the research and what can be done, to see that the quickest way may not be what to a layman might be the most direct way. And that is what happened, not immediately but very soon, in the cancer program. The work that was supported, a lot of it was work with mice and chickens, and then after 10 years that work turned out to be directly relevant to humans because the background was there.

So I think the dual system in setting the broad targets at the political level in the Congress and then having the tactics of how we get to the target decided by the scientific biomedical research community is a very good double system. And in that way I think you can target everything. That would be fine as long as you let us say that yes, the best way to get there may be with this detour.

Mr. **Fuqua**. What, though, if our targeting is off-base——

Dr. **Temin**. Well, if the targeting is off-base——

Mr. **Fuqua** [continuing]. Or if it is difficult for we as lay persons——

Dr. **Temin**. OK. But what I am trying to say is that is not a real problem as long as you insist that what is done is of scientific merit. Because what is of scientific merit is going to be of use in biomedicine somewhere. So, for example, at the time 15 years ago, the war on cancer was really premature to mount such a big program, as long as there was insistence upon scientific meritorious things—recombinant DNA technology, a lot of it came out of that; basic knowledge in immunology; basic knowledge of viruses—and then finally a base was built up so that all of that in turn came back to cancer.

Mr. **Fuqua**. How about such as orphan diseases?

Dr. **Temin**. Orphan diseases, the same way. Orphan diseases, if they were targeted, as long as the research was of high scientific merit it is going to be useful and will turn out to be related to that disease and other diseases. The important thing again is the scientific merit. Because information in biology is very easily and very widely transferrable.

Mr. **Fuqua**. Thank you. Mr. Walgren.

Mr. **Walgren**. So you don't mind quite this disease-of-the-month attack on——

Dr. **Temin**. I don't mind it at your level. I think that this is the way the American people perceive research. I don't feel it is necessary that the American people understand that assaying viruses and counting cells in the laboratory is going to directly improve their health. I think it is important that they say we want more done to prevent cancer and understand cancer, that you in Congress reflect that, and then you let us say that the best way to understand cancer is to have people counting cells in the laboratory, and this is the way that in the long run is going to give us the most information and be the most effective in controlling cancer. And we have a long history so we can say that this is what works.

Mr. **Walgren**. I see. You indicated the importance of continuing support and carryover support. Oftentimes in the Congress we get a lot of respect for the damage done when we dismantle a work force. And I am thinking of the Clinch River breeder reactor when the argument was made that, "Gee, if you stop this funding, the work force will dissipate and you will lose the skills that have been assembled." And yet, somehow or other that same appreciation in other areas has not—well, that same appreciation has not spilled over into support for investigators, and I wonder why that is.

Dr. **Temin**. Well, it is perhaps not as publicized and people try very hard to get other funding. But just to illustrate again the importance with AIDS that is occurring. There were some laboratories that weren't so successful in doing the kind of research they were doing but were still in existence. AIDS came along, and they were laboratories that had exactly the techniques and skills to work on AIDS and have made enormously important discoveries. And this is going to happen in the future, because we can't predict what is the next disease that is going to come down the pike. And of course we are talking about a lot less money than required to keep that Clinch River reactor going.

Mr. **Walgren**. It is an anomaly at that level.

Does NIH make an effort to carry funding forward?

Dr. **Temin**. No. The NIH—it would be better to have them answer directly, but no, there is not a real mechanism to carry out this thing once someone loses a grant. They can take the unexpended funds sometimes and apply them to the next year. But perhaps more of a mechanism might be useful.

Mr. **Walgren**. I was sitting here thinking when you were mentioning toxic shock that I read an article not too long ago about a view that the institutional response to the evidence on toxic shock missed the mark and that, in fact, something was going on with toxic shock that wasn't at all related to the focus on that certain——

Dr. **Temin**. Bacterium. Well, I am not a specialist on that topic, but I believe there is a scientific understanding and the real question is what is available in the market, and that that needs to be changed in terms of preventing the reoccurrence or continuing high level occurrence of that. So that is a question as so frequently happens where there is a scientific understanding of something that then to get industry and the country to change behaviors related to that is sometimes a more difficult problem. And in this cigarette smoking is much more closely related. Not cigars immediately.

Mr. **Fuqua**. Thank you.

Dr. **Temin**. But where cigarette smoking is unequivocably the cause of 40 percent of cancer deaths and most of lung cancer, and so forth, we cannot stop it. So we have this great problem of getting people to behave in healthy ways. And certainly with regards to AIDS. We think we know how to prevent the spread of AIDS now by the AIDS virus. It is clear behavioral changes, safe sex so-called, screening of blood, clean needles for drug addicts would prevent the epidemic spread. But how we get people to do these things which are healthy for them is much harder.

Mr. **Walgren**. Well, you have great confidence, though, in the ability of the institutions to derive the right lesson from the scientific evidence, and I certainly could not gainsay that. Is that not right, that you do have that confidence in the institutions?

Dr. **Temin**. Well, I think that all we can look at is the recent history, and recently I think we have done very well because we have two ways of looking at things: that one way is the political way and things are targeted broadly as we have said, and then as long as you allow us flexibility in tactics, then I think that we can operate very successfully.

Mr. WALGREN. How do you react to the merger of the facilities funding and the research grants where an argument is made that some of the allocations that the scientific community have complained about were for facilities, for bricks and mortars, and that traditionally the Congress has played a large role in the location of scientific facilities, although staying clear of allocating or directing individual research grants? Is there greater legitimacy in locating a facility——

Dr. TEMIN. No.

Mr. WALGREN [continuing]. Than there is in pursuing individual grants?

Dr. TEMIN. There is not. Again it is Congress, we believe, that should make the broad decisions about that. If Congress decides we need a new institute of material science, or we need more supercomputer facilities, I think this is a congressional prerogative and Congress should be the one to make these decisions. But the peer review system that was much criticized is the best system known. It is not perfect, but it is better than any other system we know to decide what is going to be the best place to do that. And this requires, then, proposals from people who are interested, and then a group of people who can evaluate these things—look at all these proposals, and see which should actually be the best. And with all respect for the Congress, I think it is best for scientists to make that kind of decision, while the Congress makes the broad political decision that, "Yes, we need to do more in this area."

Mr. WALGREN. And that would especially apply to Defense Department moneys as well. In fact, if you were to run the range of dollars committed, the attack probably should be sharper on the defense community for not following strict peer review in their allocations.

Dr. TEMIN. I think that if one could put this at the Congress, if the Congress—this is outside my area, but if Congress decided upon broad defense policy issues rather than hardware, and then said to the Congress that we needed to have two or two and a half ocean navies, and an army here and there, and defend here and there, and let then those people decide how best to carry out these goals, I believe that would be a much more efficient system. That is the system that we have primarily used in science, and it has been enormusly successful. I think it could be generalized as you state.

Mr. WALGREN. Thank you, Mr. Chairman.

Mr. FUQUA. Dr. Temin, thank you very much for being with us this morning. We appreciate your contributions. Thank you very much.

[Whereupon, at 10:05 a.m., the task force was adjourned, to reconvene at 10 a.m. on Wesnesday, April 23, 1986.]

[Questions and answers for the record follow:]

McARDLE LABORATORY
FOR CANCER RESEARCH
DEPARTMENT OF ONCOLOGY
MEDICAL SCHOOL, UNIVERSITY OF WISCONSIN

April 24, 1986

RECEIVED
APR 29 1986
COMMITTEE ON SCIENCE
AND TECHNOLOGY

Congressman Don Fuqua
Committee on Science and Technology
U.S. House of Representatives
Suite 2321 Rayburn House
Office Building
Washington, D.C. 20515

Dear Congressman Fuqua:

I was glad to appear before the Task Force on April 22. I was sorry there was not more time for questions. Since I had a copy of possible questions, I am taking this opportunity to give you an indication of what my answers would have been.

First, however, I want to clarify my statement about targeting. It was pointed out to me that I might not have been clear in responding to you. When I was stating that I felt Congress should target research, I was suggesting fairly broad goals like research against cancer, heart disease, etc. I was not suggesting targeting at a very specific level. I feel that within the large target specified by Congress, the biomedical research community should set out the means of approach. For example, if AIDS had appeared 25 years ago, the best approach to AIDS would have been to study chicken retroviruses, not to work on AIDS directly.

On page 11 of the suggested questions No. 1 relates to the young investigators. I think that the scientific community is now much more aware of this problem and that there are mechanisms to assure funding of good research proposals from young investigators. Young investigators usually do have an advocate in that the senior people in their departments or institutions help them and guide them. In the case of McArdle Laboratory, we even supply the money for the early research by young investigators in our department.

No. 2 about targeting was discussed. I feel that we should target a lot of what we are doing, but that some of the approaches to reaching the target in fact most of them should be nondirected. When we know how to do something, like make a new vaccine, then we can directly do it. When we don't know if the vaccine is useful, we need to do basic research to determine that first.

No. 3 is about the sources for other funding. The private sector is not likely to support unorthodox, innovative ideas. The private sector is controlled by business motivations which have to be quite short-term. Even in the largest companies 5-10 years is a very long time. This is a relatively short time in science. There is going to be a great problem for science in the cutoff of federal funding. Since it is very hard to predict what will be signifi-

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608-262-2177

can't because if we knew it would already be done, whatever research is not done is a problem.

No. 4 is about the interaction between basic researchers and clinicians. This is not as much of a problem as it appears. Clinicians in this country are very eager to intervene to benefit their patients. Thus, we find that they are frequently besieging us to rush things into usefulness for them. As long as we have strong medical schools I think that this interaction will continue.

No. 5 relates to focusing attention and resources toward solving problems; again AIDS is a good example, even if we focused all of our resources on AIDS 20 years ago, we should not have gotten very far because we didn't know anything about retroviruses. This is still true with many other areas of biology. We need to have a broad knowledge base so that when health problems arise we can move closer to an answer. In terms of developing drugs against the virus of AIDS, a knowledge base in computer modeling and medicinal chemistry needs to be improved to succeed in this aim.

No. 6. The changes in the structure of biomedical research will continue. However, as long as we have study section mechanism, I hope there still will be support for smaller laboratories. Frequently the innovative ideas come from the smaller laboratories and thus it is important that a balance be kept between large and small laboratories. The study section mechanism seems to be doing this.

No. 7 relates to long-range planning. I think it is realistic to set a continued base level of support for biomedical research which should be some percentage of the total government expenditures on health or the total U.S. expenditures on health. It is only prudent to spend on research to improve health while at the same time delivering health care. When there are limited federal funds, it may be more important that all really good scientists be supported since there are in addition to federal funds other non-federal funds which can supplement and insure that the best scientists are fully supported.

I hope these comments are useful and I would be glad to give any further counsel to the best of my ability.

With best regards,

Sincerely yours,

Howard M Temin

Howard M. Temin

HMT/kal

SCIENCE POLICY TASK FORCE

Hearings on Policies for Biomedical Research

April 22, 1986

Questions for Dr. Howard M. Temin

1. With regard to receiving your first grant, you and the U.S. scientific community have been extremely fortunate that you succeeded. In your experience, have deserving young investigators who propose sound, albeit innovative research projects today been as fortunate? Do they need an advocate to assure their chances of funding support?

2. From your perspective, is it possible to determine which projects will yield results and lead to successful clinical applications? Should there be a balance between targeted and non-directed programs, and how should the balance be weighted?

3. As Federal funding for research becomes tighter, are other sources in the private sector likely to support unorthodox, innovative ideas? Is there the possibility that certain research will not be funded unless it fits into the mainstream? What will be the significance of this for U.S. science in the short term? In the long term?

4. With the illustration of AIDS, you cite the importance of the interaction between the basic researcher and the clinician in biomedical research. Will this cross fertilization of ideas and approaches be jeopardized by the increasing trend of fewer clinicians in research? If so, what suggestions can you offer for reversing this trend?

5. In your view, will focusing public attention and resources on particular health problems, such as AIDS, lead to more rapid, effective solutions? Is this strategy always successful?

6. You indicate and provide evidence for changes in the structure of biomedical science in the U.S. with more investigations and more cooperation between investigators. In your view, will this trend continue as the science base enlarges and experiments may be more complex and costly to perform? If so, how will this affect the way biomedical research is performed in the long term? How will this affect the lone investigator from the standpoint of being able to compete?

7. You indicate that there is a lack of long-range planning or of consideration of long-range effects on maintaining the strength and continuity of the biomedical research community. You offer some suggestions in this regard. In your view, is it realistic to set a continued base level of support for biomedical research? If so, what criteria should be considered in this regard? Should all good scientists be supported, or should the best scientists be adequately supported?

POLICIES FOR BIOMEDICAL RESEARCH

WEDNESDAY, APRIL 23, 1986

House of Representatives,
Committee on Science and Technology,
Task Force on Science Policy,
Washington, DC.

The task force met, pursuant to call, at 10 a.m., in room 2318, Rayburn House Office Building, Hon. Doug Walgren (acting chairman of the task force) presiding.

Mr. Walgren. Why don't we begin, because we have a number of very good contributors to the task force's proceedings today.

As some of you know, today is the second of three hearings on policies for biomedical research. Yesterday, Dr. Luria provided an overview of Federal biomedical research programs, and talked about general policy issues that affect this area. Dr. Rall and Dr. Raub focused on the Intramural and Extramural Research Programs at NIH, commenting on their merits and the contributions that they make to biomedical research. Dr. Moskowitz described program evaluation at NIH, and emphasized the importance of maintaining quality of research and the contribution that the program evaluation makes toward that. Dr. Temin talked of Federal research programs from the perspective of the individual investigator and the university, particularly emphasizing the importance of continuity and consistency and predictability in our research effort if we are to maintain the quality and the leadership that we presently have as a society.

Today we want to explore the evaluation of research benefits in the biomedical area, particularly focusing on the transfer of basic research information to application in clinical medicine and also impact on public health areas.

We will hear first from Dr. Paul Marks, the president and chief executive officer of the Memorial-Sloan Kettering Cancer Center, and then Dr. Howard Hiatt, professor of medicine at Harvard University's Brigham Young and Women's Hospital, and the former dean of the Harvard School of Public Health; also Dr. Richard Greene, Director of Medical Research Service of the Veterans' Administration; Dr. Shervert Frazier, the Director of the National Institute of Mental Health; and Dr. Donald Fredrickson, the president and chief executive officer of the Howard Hughes Medical Institute; and, as most of you remember, Dr. Fredrickson was a former Director of the National Institutes of Health.

Well, gentlemen, we appreciate your being a resource to our process, and we welcome you to the proceedings.

Any written statements that witnesses would like to submit would be welcome and certainly will become part of our record, and you can feel free to focus or discuss the points you'd like to make in whatever way is most effective for you.

So welcome to our proceedings, Dr. Marks. We're glad you're here, and we'd be pleased to have you give us your views in this area.

STATEMENT OF DR. PAUL MARKS, PRESIDENT AND CHIEF EXECUTIVE OFFICER, MEMORIAL-SLOAN KETTERING CANCER CENTER, NEW YORK, NY

Dr. MARKS. Thank you very much, Mr. Walgren.

As you indicated, I am currently president and chief executive officer of Memorial-Sloan Kettering Cancer Center, a position I've held since 1980. Prior to that, I was vice president for health sciences at Columbia University. I served as a member of the President's Biomedical Research Panel in 1976, the President's Cancer Panel from 1976 to 1979, and I'm currently a member of the Council of the United States National Academy of Sciences.

I appreciate this opportunity to testify before you, and I applaud your initiatives in going forward with this careful review of our Nation's science policy.

The role of the Federal Government, particularly since the end of World War II, has been very significant in the development of new technologies in the life sciences. Biomedical research and development in the United States today would not be where it is without the substantial funding of research, particularly through the National Institutes of Health, constantly supported through the Congress. The substantial constraints that face the future funding of biomedical research and development are a matter of concern. This is due, in part, to the specter of lost opportunity to exploit the advances in biomedical research that have been achieved during the past several years.

Have we appropriately defined our national goals for the new biomedical technologies in terms of the health of our people as well as our economic well being? I do not believe that we have.

I have been requested to focus my remarks first on the evaluation of research benefits and, second, on what will be important to assure the transfer of basic research information to clinical practice. My difficulty is to extract a few salient points relative to this broad mandate.

First I was asked to briefly describe the Memorial-Sloan Kettering Cancer Center. This Center is the oldest privately-operated nonprofit institution devoted to research, education, and patient care in cancer. The Center has two operating organizations—the Memorial Hospital, which is a 565-bed facility, and the Sloan Kettering Institute. We have a clinical staff of some 345 M.D.'s, almost all of whom are involved to some extent in clinical research, and approximately a fifth of them commit a substantial portion of their effort to clinical or laboratory investigation. Basic research in our Center proceeds across-a-broad spectrum of biomedical sciences and is carried out under the leadership of 129 full-time members of the scientific staff.

One of the hallmarks of our center is an institutional commitment to close collaboration between laboratory sciences and physicians working at the bedside. The Center's education programs provide research and clinical training at the graduate and post-graduate levels as part of the graduate school of Cornell University which offers the Ph.D. degree, programs toward the M.D./Ph.D. degree, and rather extensive programs for training at the post-doctoral research and clinical levels.

Our total operating budget projected for 1986, which includes patient care, research, and education, is approximately $320 million, of which about $70 million is in support of research. Federal grants provide 65 percent of the research support, the vast majority representing RO and PO research grants from the NIH; 30 percent of our research support derives from foundations and private philanthropy. Support from industry represents only 6 percent, and over the past 5 years this support from industry has increased fivefold, although it has been essentially level for the past couple of years. This level of funding by industry is about the national average—namely, 5 to 6 percent. Guidelines for industrial collaborations have been developed which, we believe, preserve the values and priorities of our academic institution——

Mr. **Walgren**. That bell will stop, and we can just continue.

Dr. **Marks**. Right—which have made possible the progress we stand ready to exploit while recognizing the interests and goals of industry. I will return to the potential for increased industry-academic collaboration in a moment.

Our Center places a high priority on monitoring all of our programs to assure that they are of high quality and productivity. These internal rigorous monitoring procedures and policies are similar to those at other leading research based academic institutions.

Turning specifically to the issue of evaluating research benefits, the agenda for this science policy review indicates your desire that the definition of the issues, and enunciation of recommendations permit quantitative approaches to be brought to bear when possible. This is certainly desirable, but this probably cannot be done as part of a prospective evaluation of support for basic biomedical research on a program-by-program basis. By its very nature, basic research is the pursuit of new knowledge whose course cannot be predicted and cannot be planned. The critical elements in evaluating basic research are the individual scientist's imagination and creativity and the importance of the questions being asked. On the other hand, we can come closer to a quantitative evaluation of the potential of applied research which frequently is characterized by carefully planned pursuit of a well-defined goal. Applied biomedical research is carried out to some extent in academic institutions, but in this country it has been primarily a function of the industrial sector.

One can evaluate the benefits of biomedical research by several parameters, for example, an enumeration of diseases which were previously incurable that can now be prevented or cured, the number of new products that have been developed as effective treatment for disease, or the impact of biomedical research and development on our economic growth.

The report of the President's Biomedical Research Panel in 1976 concluded—and I quote—that "the successes of the last three decades portend an acceleration in the pace of discovery in the immediate and distant future." The remarkable biomedical base of our Nation "is an indispensable resource. This science base provides the only sound basis for learning how to prevent and control disease."

These statements in 1976 have been exceeded far beyond all of our then-optimistic predictions. We have witnessed advances in biomedical sciences over the last decade which are truly remarkable. Two areas stand out. One is based on recombinant DNA technology. The other is immunology, in which cancer cells are fused with antibody-producing white blood cells to form hybridomas which produce monoclonal antibodies. In terms of new products, these technologies are likely to be responsible for a long list, including vaccines, hormones, enzymes, growth factors, and so forth. They have already led to some 15 or 20 products now in various stages of clinical trials. These new agents have application for dissolving blood clots in treating coronary occlusion and strokes, vaccines to prevent malaria and chicken pox, hormones that stimulate white blood cells and mobilize the body's defenses against disease, and biological agents to treat cancer. Two products, human insulin and human growth hormone, are already being marketed.

In the area of curing disease, the list is ever lengthening. For example, in my own area, substantial advances have been made in our ability to cure testicular cancer, childhood acute leukemia, Hodgkin's disease, all formerly almost uniformly fatal and all curable now in 60 to 90 percent of cases in early stages of the disease.

In economic terms, the past decade has seen the growth of a multibillion-dollar industry based on new biotechnologies, an industry which represents perhaps one of the fastest growing sectors of our economy.

Turning now to address what is important to assure the appropriate and necessary transfer of basic research information to clinical practice, I will briefly discuss three requirements that are particularly critical for the process to work well.

The R&D process from basic research to the marketing of a useful new product must involve a partnership among Government, academic, and industrial institutions. To flourish, the enterprise needs reasonably adequate funding and a continuing source of talented and well-trained young men and women.

Biomedical research and development has two main goals—the generation of fundamental knowledge, and the development of new useful products. New products result from the application and development of new knowledge, and the perceived need for new products may provide an important impetus to the search for new knowledge. I don't believe it is useful to argue about which aspect of the continuum of the research development process is most important, since all are required. For example, in the glitter and glamor of recombinant DNA technology one may lose sight of the fact that many steps requiring hard work are involved in the development of a pharmaceutical product. After learning how to produce a product, there is a complex process of preclinical and clinical testing to determine how to use it effectively. Evaluation of a drug's scope of efficacy and side effects requires the collaboration of many disciplines. Laboratories of basic biological research must be in good contact with their clinical colleagues, and the industrial sector must interact with both, for the most productive application of basic research. It behooves all of us concerned with the vitality of biomedical research in this country to ensure that all aspects of the process are appropriately interactive, intelligently administered, and adequately supported.

I recognize that in addressing the issues of funding of biomedical research, I do so in the context of the substantial economic constraints facing our Government. What is an appropriate level of Federal support for basic biomedical research? In 1984, the total support for biomedical research in the United States was estimated to be in the range of $8–$9 billion. Of this $8–$9 billion, $2.5 billion represented support from the National Institutes of Health, and only an estimated $170 million represented industrial support for basic biomedical research in academic institutions.

The Federal Government is, and will continue to be, by far the major source of funding for basic biomedical research. According to the Office of Management and Budget, in 1987 the total Federal obligations for all types of research and development is projected at $63 billion, an increase of 16 percent above 1986 estimated levels. Nevertheless, the projected 1987 budget for the National Institutes of Health calls for a 5-percent decrease below 1986 levels. In the context of the current rapid advances in biomedical research and the opportunities for exploiting these advances in terms of further expanding our fundamental knowledge, as well as application in health care and health maintenance, a high priority should be to provide for reasonable growth in the Federal commitment to support biomedical research. Because of the potential benefits to the health of our Nation and to our economic prosperity, an increment in funding for biomedical research and development in the Federal budget should be in line with the overall projected increase in Federal obligations for all research and development above the 1986 level. Biomedical research is very vulnerable to instability of support. Active research teams once disbanded cannot easily be reassembled, and loss of access to the most advanced equipment is often the difference between world-class and second-rate research.

Industry should also be encouraged to increase its support of academic biomedical research and to increase the proportion of this support that represents long-term commitments to fund research and training. Industry cannot flourish unless there is a continuing flow of trained scientists, clinicians and other technicians, as well as a continuingly expanding base of fundamental knowledge. The Government has a role to play in fostering the expansion of academic-industrial partnerships. The President's Commission on Industrial Competitiveness recommended that the Government consider measures, including appropriate tax credits, for corporate support of academic biomedical research. A more effective partnership among industry, academia, and Government in the support of biomedical research is also important in the context of competition we face. High-technology industries from abroad have already come looking to the U.S. academic institutions to exploit our basic biomedical knowledge base.

Another important aspect of the transfer of basic research information to clinical practice is the continuing access to a pool of well-trained young scientists and clinicians. The clinician scientist is critical to the continuum of biomedical research and development. The interface between basic laboratory research and clinical investigation requires the M.D. investigator in the research and development process. Various studies have indicated that the number of M.D.'s trained in science and entering biomedical research has been declining over the past several years. We must be able to attract an increased proportion of M.D.'s into biomedical research and development. An important factor contributing to the decrease in attractiveness of biomedical R&D for M.D.'s is the uncertainty and instability of support for research. Stable support for the training of young scientists and clinician scientists deserves a very high priority, for upon them rests a large measure of the future success of the entire enterprise.

In conclusion, I would suggest for your consideration the following.

One, a reasonable rate of increase in Federal funding of biomedical research and development is required to exploit the unprecedented opportunity for new and effective products for definitive treatment of a broad range of diseases and interventions that will be effective in preventing disease and maintaining health. Definitive prevention and treatment of disease are the most cost-effective approaches to the maintenance of the health of our people.

Two, Federal support of biomedical research and development must involve full public accountability. A most important aspect of public accountability is assurance that the process for allocation of funds in support of biomedical research and development identify programs of the highest quality both in extramural and intramural federally supported programs.

Three, the Federal Government should encourage increased interaction and collaboration between academia and industry.

Four, there should be a continuing commitment to adequately support the training of basic and clinical scientists who are critical to the long-term success of biomedical research.

And, five, measures to increase the stability of funding, such as longer-term grants, are desirable. This is consonant with the long-term nature of basic biomedical research. Such measures could contribute to decreased administrative costs as well increased efficiency and productivity of our research programs.

I thank you.

[The prepared statement of Dr. Marks follows:]

Testimony Before The
Task Force on Science Policy
Committee on Science and Technology
Don Fuqua, Florida, Chairman

"Policies for Biomedical Research"
Paul A. Marks, M.D.
President
Memorial Sloan-Kettering Cancer Center
New York, New York
April 23, 1986

4/22/86

My name is Paul A. Marks. I am a physician and cell biologist whose primary research interest has been in the area of normal and cancer cell differentiation. I am President and Chief Executive Officer of Memorial Sloan-Kettering Cancer Center, a position I have held since October 1980. Prior to that I was Vice President for Health Sciences, Columbia University, Director of its Comprehensive Cancer Center and Professor of Medicine and Human Genetics. I served as a member of the President's Biomedical Research Panel in 1976, the President's Cancer Panel from 1976 to 1979 and am currently a member of the Council of the U. S. National Academy of Sciences.

I thank the Committee for this opportunity to testify before you with respect to policies for biomedical research. I applaud your initiatives in going forward with this careful review of our nation's science policy to gain a deeper understanding of past policies, present problems, as well as future needs and choices in keeping America strong in science.

The role of the federal government, particularly since the end of World War II, has been very significant in the development of new technologies in the life sciences. Biotechnology in the United States today would not be where it is without the substantial funding of research and development by the National Institutes of Health, constantly supported through the Congress. The substantial constraints that face the future funding of biomedical research and development are a matter of concern. This is due, in part, to the spector of lost opportunity to exploit the advances in biomedical research that have been achieved in the past several years.

Have we appropriately defined our national goals for the new biomedical technologies in terms of the health of our people, as well as our economic well-being? I do not believe that we have.

I have been requested to focus my remarks first on the evaluation of research benefits and secondly on what will be important to assure the transfer of basic research information to clinical practice. My difficulty is to extract a few salient points relevant to this broad mandate.

Brief Description of Memorial Sloan-Kettering Cancer Center

I was asked to briefly describe the Memorial Sloan-Kettering Cancer Center. This Center is the oldest, privately operated nonprofit institution devoted to research, education and patient care in cancer. The Center has two operating organizations - the Memorial Hospital, a 565 bed facility, and the Sloan-Kettering Institute for Cancer Research. We have a clinical staff of 345 M.D.s, almost all of whom are involved to some extent in clinical research and approximately a fifth of whom commit a substantial portion of their effort to clinical and/or laboratory investigation. Basic research in our Center proceeds across a broad spectrum of the biomedical sciences and is carried out under the leadership of 129 full members of our scientific staff. One of the hallmarks of the Memorial Sloan-Kettering Cancer Center is our institutional commitment to close collaboration between laboratory scientists and physicians working at the bedside. The Center's education programs provide research and clinical training at the graduate and postgraduate levels. As part of the graduate school of Cornell University, we offer the Ph.D. degree in biological sciences, and a program leading to the M.D.-Ph.D. degrees, as well as programs of training for postdoctoral research and clinical fellows and other health professionals. Our total operating budget projected for 1986 is approximately $320,000,000 of which about $70,000,000 is in support of our research programs. Federal grants provide 65% of the research support, the vast majority representing RO and PO research grants from the National Institutes of Health, 30% of our research support comes from foundations and private philanthropy. Over the past five years support from industry has increased fivefold, but still represents only 6% of our total research expenditures and has been essentially at this level for the past two years. Of the total funding for biomedical research in academic institutions, the national average for the proportion supported by industry is 5% to 6%. Guidelines for our industrial collaborations have been developed which, we believe, preserve the values and priorities of our academic institution which have made possible the progress we stand ready to exploit, while recognizing the interests and goals of industry. The Center places a priority on monitoring all of our programs to assure that they are of high quality and productivity. These internal, rigorous monitoring procedures and policies are similar to those at other leading research based academic institutions.

Evaluation of Research Benefits:

Turning specifically to the issue of evaluating research benefits, the agenda for this Science Policy Review indicates your desire that the definition of the issues, and enunciation of recommendations permit quantitative approaches to be brought to bear when possible. This is certainly desirable but this probably cannot be done as part of a prospective evaluation of support for basic biomedical research on a program by program basis. By its very nature, basic research is the pursuit of new knowledge whose course cannot be predicted and cannot be planned. The critical element in evaluating basic research is the individual scientist's imagination and creativity. On the other hand, we can come closer to a quantitative evaluation of the potential of applied research which frequently is characterized by a carefully planned pursuit of a well defined goal. Applied biomedical research is carried out to some extent in academic institutions but in this country it has been primarily a function of the industrial sector.

One can evaluate the benefits of biomedical research by several parameters - these include, for example, an enumeration of diseases which were previously incurable that can now be prevented or cured; the number of new products that have been developed as effective treatment for disease; and the impact of biomedical research and development on our economic growth.

The report of the President's Biomedical Research Panel in 1976 concluded that "the successes of the last three decades portend an acceleration in the pace of discovery in the immediate and the distant future...." The remarkable biomedical science base of our nation "is an indispensable resource. This science base provides the only sound basis for learning how to prevent and control disease." Far beyond all of our then optimistic predictions, we have witnessed advances in biomedical sciences over the last decade which are truly remarkable. Two areas stand out. One is based on recombinant DNA technology. The other is immunology in which cancer cells are fused with antibody producing white blood cells to form hybridomas which produce monoclonal antibodies. In terms of new products, these technologies are likely to be responsible for a long list including vaccines, hormones, enzymes, growth factors and so forth. They have already led to some fifteen or twenty products which are in various stages of clinical trials. These new agents have application for dissolving blood clots in treating coronary occlusion and strokes, vaccines to prevent malaria and chicken pox, hormones that stimulate white blood cells and mobilize the body's defenses against disease and biological agents to treat cancer. Two products, human insulin and human growth hormone, are already being marketed.

In the area of curing disease the list is ever lengthening. For example, in my own area substantial advances have been made in our ability to cure testicular cancer, childhood acute leukemia, Hodgkins disease, all formerly almost uniformily fatal and all curable now in 60% to 90% of cases in early stages of the disease.

In economic terms, the past decade has seen the growth of a multi-billion dollar industry based on the new biotechnologies, an industry which represents perhaps one of the fastest growing sectors of our economy.

Requirements for transfer of basic research information to clinical practice:

Turning now to address what is important to assure the appropriate and necessary transfer of basic research information to clinical practice, I will briefly discuss three requirements that are particularly critical for the process to work well.

The R&D process from basic research to the marketing of a useful new product must involve a partnership among government, academic and industrial institutions. To flourish the enterprise needs reasonably adequate funding and a continuing source of talented and well-trained young men and women.

Biomedical research and development has two main goals - the generation of fundamental knowledge and the development of new useful products. New products result from the application and development of new knowledge. The perceived need for new products may provide an important impetus to the search for that knowledge. It is not useful to argue about which aspect of the continuum of the research and development process is most important, since all are required. For example, in the glitter and glamour of recombinant DNA technology one may lose sight of the fact that many steps, requiring hard work, are involved in the development of pharmaceutical products. After learning how to produce a product we must determine how to use it effectively. Evaluation of a drug's scope of efficacy and side effects require the collaboration of many disciplines. Laboratories of basic biological research must be in good contact with their clinical colleagues and the industrial sector must interact with both, for the most productive application of basic research. It behooves all of us concerned with the vitality of biomedical research and development in this country to insure that all aspects of the process are appropriately interactive, intelligently administered and adequately supported.

I recognize that in addressing the issues of funding of biomedical research and development, I do so in the context of the substantial economic constraints facing our government. What is an appropriate level of federal support for basic biomedical research? It is hard to derive a precise figure for the current level of biomedical research support in this country. In 1984, the NIH budget was $4.26 billion and it was estimated that the pharmaceutical industry spent $3.1 billion for human and vetinerary R&D. Allowing for approximately another 1 to 2 billion from other government agencies, non pharmaceutical companies, and various other private sources, total support for biomedical research and development in the United States in 1984 was somewhere in the range of $8 to $9 billion. Of this $8 to $9 billion, $2.5 billion represented support from the National Institutes of Health and only $170 million represented industrial support for bioimedical research in academic institutions.

The federal government is, and will continue to be, by far the major source of funding for basic biomedical research. According to the of the Office of Management and Budget, in 1987, the total federal obligations for all type of research and development is projected at $63 billion, an increase of almost $9 billion or 16% above 1986 estimated levels. Of this amount, $2.9 billion is targeted for NIH support of R&D in academic institutions. This projected budget for the National Institutes of Health represents a 5% decrease below 1986 levels. In the context of the current rapid advances in biomedical research and the opportunities for exploiting these advances in terms of further expanding our fundamental knowledge, as well as application in health care and health maintenance, a high priority should be to provide for reasonable growth in the federal commitment to support biomedical research and development. Because of the potential benefits to the health of our nation and to our economic prosperity, an increment in funding for biomedical research and development in the federal budget should be in line with the overall projected increase in federal obligations for all research and development above the 1986 level. Biomedical research is very vulnerable to instability of support. Active research teams once disbanded cannot easily be reassembled. Loss of access to the most advanced equipment is often the difference between world class and second rate research.

Industry should also be encouraged to increase its support of academic biomedical research and development and to increase the proportion of this support that represents long-term commitments to fund research and training. Industry cannot flourish unless there is a continuing flow of trained scientists, clinicians and other technicians, as well as a continuing expansion in our fundamental knowledge base. The government has a role to play in fostering expansion of academic-industrial partnerships. The President's Commission on Industrial Competitiveness recommended that the government consider measures, including appropriate tax credits, for corporate support of academic biomedical research and development. A more effective partnership among industry, academia and government in the support of biomedical research and development is also important in the context of competition we face. High technology industries from abroad have already come looking to the United States' academic institutions to exploit our biomedical knowledge base and product potential.

To digress for a moment, I recognize that partnerships between academia and industry are not without potential problems. Appropriately, the missions and goals of academia and industry differ. Partnerships may require certain changes in the way each of the partners have traditionally seen their priorities and carried out their mandates. We must preserve the basic value system of our academic institutions, a value system upon which depends the very progress we now wish to exploit. Nevertheless our challenge is not to resist change but to manage it so that we can continue to flourish through the expansion of our knowledge, the quality of our teaching and the effectiveness by which we transfer technology to benefit society. No change, no matter how worthwhile, is without risk. We face challenges that can be opportunities to forge new partnerships to maintain and strengthen biomedical research and development in this country.

The third important factor for the transfer of basic research information to clinical practice is continuing access to a pool of well trained young scientists and clinicians. The clinician scientist is critical to the continuium of biomedical research and development.The interface between basic laboratory research and clinical investigation and clinical application requires the M.D. investigator in the research and development process. Various studies have indicated that the number of M.D.s trained in science and entering biomedical research has been declining over the past several years. For example, in 1982, only 40% of medical school faculty who served as principal investigators on research grants from the National Institutes of Health were M.D.s compared to approximately 55% in 1972. This trend appears to be continuing. We must be able to attract an increased proportion of M.D.s into biomedical research and development. An important factor contributing to the decrease in attractiveness of biomedical R&D for M.D.s are the uncertainty and instability of support for research. Stable support for the training of young scientists and clinician scientists deserves a very high priority, for upon them rests a large measure of the future success of the entire enterprise.

In conclusion, I would suggest for your consideration the following:

1. A reasonable rate of increase in federal funding of biomedical research and development is required to exploit the unprecedented opportunity for new and effective products for definitive treatment of a broad range of diseases and interventions that will be effective in preventing disease and maintaining health. Definitive prevention and treatment of disease are the most cost effective approaches to the maintenance of the health of our people.

2. Federal support of biomedical research and development must involve full public accountability. A most important aspect of public accountability is assurance that the process for allocation of funds in support of biomedical research and development identify programs of the highest quality both in extramural and intramural federally supported programs.

3. The federal government should encourage increased interaction and collaboration between academia and industry.

4. There should be a continuing commitment to adequately support the training of basic and clinical scientists who are critical to the long-term success of biomedical research and development.

5. Measures to increase the stability of funding, such as longer term grants, are desirable. This is consonant with the long-term nature of basic biomedical research. Such measures could contribute to decreased administrative costs, as well as increased efficiency and productivity of our research programs.

DISCUSSION

Mr. **Walgren**. Thank you very much, Dr. Marks.

I apologize. At this point we'll have to suspend, and I'll go and respond to these bells and come right back, and I hope you can stay with us and we can talk a little bit further.

[Recess.]

Mr. **Walgren**. Let's reconvene.

Let's see what can be said here. Are there any other suggestions that could be made about increasing our ability of technology transfer? We apparently are doing a lot of the basic research and we have a pretty vital information developing system, and yet other countries do seem to be able to take that information from us and proceed down the development process a little bit more expeditiously than we do. Is there any other thought you'd like to raise specifically on technology transfer that would help us in that area?

Dr. **Marks**. I think that there probably are other things that can be done to facilitate this technology transfer. Certainly one of the areas, I think, of concern right now in technology transfer has to do with the introduction of products of recombinant DNA which, on the whole, are frequently naturally occurring substances, into clinical trials, and it's been our experience at least that there is room to improve the interaction among the various Federal agencies—the FDA, the NIH—as well as academic institutions and industry in this area.

Specifically, we recently had experience at Memorial with a substance called tumor necrosis factor which has substantial interest in application for the treatment of cancer. It was a substance discovered at Memorial. To make a very long story short, a Japanese company was the first to bat with cloning the gene and producing enough to enter into clinical trials. Initially, it was offered to several U.S. companies, and they were reluctant to go forward.

I think this whole area of exploitation of biologicals carries with it considerations in terms of increased sorts of risks above simple chemicals which must be a concern in terms of both the issues related to structuring clinical trials all the way to the whole issue of liability.

Mr. **Walgren**. Why were those companies reluctant to go forward?

Dr. **Marks**. Well, I think that traditionally—you know, this was, say, 3, or 4, or 5 years ago; tumor necrosis factor was one of the early products of the contemporary technologies. There was the perception that biologicals are an area which are extremely difficult to evaluate in terms of clinical efficacy as well as toxicity. These substances generally carry with them greater risk in terms of side effects, in terms of the criticality of purity of these substances, and so on.

The whole area of vaccines—vaccines is an example of these biologicals—as you know, is an area of substantial concern in this country because of the fact that there aren't a lot of parties to the development and production of many vaccines because of the perceived high risk/low return of some of these biologicals.

Mr. **Walgren**. With respect to basic research in particular, is the fact that a foreign country is the one that puts it in everyday use damaging to our scientific position with respect to the strength of our basic research, or is that damage limited to the fact that there are not some economic opportunities in the United States that there would otherwise be?

Dr. **Marks**. I think it is just not limited to the economic issues, because as I tried to indicate, during the period of development, or clinical trials, which I would consider a part of the development process, there is a continuing interaction between the progress being made at a basic level with respect to the product, and its area of application and the clinical experience. This is a feedback which generally results in expanding our basic knowledge base and fine-tuning, if you will, the evaluation of efficacy and toxicity of a clinical product.

Again, taking the tumor necrosis factor as an example, we are now working with an American company to evaluate the clinical efficacy of this substance, and there is no question that the interaction is benefiting not only the potential economic exploitation of this product, but right now even more importantly, expanding our knowledge basis. So there is clearly this feedback potential which has, I think, very important advantages, and without being overly chauvinistic, it clearly is both easier and I think in the long-term interest of this country, better, to see this interaction between American academic institutions and American industry.

Mr. **Walgren**. You mentioned the importance of the basic researcher and a clinical investigator, or a bedside physician and a laboratory scientist being in close interaction with each other. Are there other suggestions other than the stability of funding that could be made to increase that contact in our system? I gather fewer physicians are pursuing purely scientific or closely research-oriented practices or suits.

Dr. **Marks**. Right.

Mr. **Walgren**. Is it because there aren't enough institutions in our society where that kind of work is being done. How can we increase it?

Dr. **Marks**. I don't think the potential number of institutions that are sites for this type of appropriate and intimate interaction is the limiting factor. I do think that many of these institutions are having trouble supporting, not only the training of these individuals, but young scientists and clinician scientists in getting started in their own independent careers.

Mr. **Walgren**. So it really is just a thinness of the fundamental support in the system for research?

Dr. **Marks**. I think this is largely the limiting factor right now for young people in the research enterprise.

Mr. **Walgren**. As you know, we have been having this flap about indirect costs——

Dr. **Marks**. Right.

Mr. **Walgren** [continuing]. And the attempt to, I gather, the attempt to reduce indirect cost is simply to make the research dollar more efficient or more productive in a research vain. What is your sense for the indirect cost problem? Is it one where we are losing lots of money that would otherwise be available to strengthen the actual supportive research, or is this something that is not a valid distraction to us if we are really concerned about strengthening research?

Dr. **Marks**. I think I can make several points with regard to that. First, much of indirect cost is really a true and integral cost of doing research. Second, you can restructure that cost base, but if it is a true and integral part of the cost of doing research, you are not going to eliminate it. In other words, you can put more of it into a direct up-front cost of the research so that you know what you are getting for your dollar more explicitly.

It is, I think, extremely important as we go forward with examining and reordering our approach to indirect cost reimbursement that we, up-front, understand that the institutions which are vital resources to doing biomedical research in this country are critically dependent upon adequate indirect cost recovery, because they are, as I said, true costs to the institution of providing the base for this research. Having said all this, I do think that probably increased efficiencies can be achieved, and that it is certainly worthwhile to rigorously examine the indirect cost structure on an institution-by-institution basis. I think that certain incentives and motivations can be introduced to decrease indirect costs, like greater interinstitutional collaboration, particularly with regard to what might be called big-ticket items in biomedical research; greater interinstitutional collaboration in various administrative matters, such as computer centers or libraries which are usually major contributors to indirect costs, and also greater interinstitutional collaboration in certain aspects of our training programs. I think that these are reasonable, valid and appropriate, but I do believe that capping indirect costs may be counterproductive. I think that one has to go at it really on an institution-by-institution basis, but I do think there is money to be saved, so to speak, and transferred to the direct research cost probably in that area.

Mr. **Walgren**. Where do you think industry support of university research is going? You say it has been at 5 percent for the last 2 years, and that is not a very large percentage. Do you anticipate it increasing substantially?

Dr. **Marks**. The last word threw me.

I anticipate it increasing. I see more and more a number of the really major leading pharmaceutical companies developing programs to support basic biomedical research and training, and also developing these programs along lines where quality is the driving force, where they are willing to commit funds in a relatively unrestricted fashion, whose use is primarily determined by the priorities set by the recipient institution.

Having said that, I would say that if industry support for academic institutions were to reach a level of, say, somewhere in the neighborhood of 8 to 10 percent of the total funded biomedical research in academic institutions, that would be a very substantial increase. I doubt very much that it will be able to grow much beyond that, because the mandates perceived by industry for their role are different from academic institutions, which I think are totally appropriate.

Mr. **Walgren**. Do you have any real apprehensions about the impact of greater industry participation on the goals of academic or basic research institutions?

Dr. **Marks**. Well, I have concerns, but I think we can manage them. It has been my experience in our institution, certainly where we have had a commitment to markedly increase industrial support, as I have indicated, and it has increased, as I said, about five fold, which in absolute dollar terms, represents an increase from about $1.5 to, say, $6 million, out of a total research budget of about $70 million.

We faced a number of problems, problems of secrecy, the problems of trying to direct the priorities of our programs, issues related to compensating our faculty involved in these collaborations, issues related to what individual faculty members would receive in terms of proportion of royalties to the institution and so on.

I would say the bottom line, and I would be glad to share in detail all of the ways we have approached these issues—and we have developed a manual about 2 inches thick which we distribute to all faculty members and potential industrial partners—the bottom line is that it can be managed, and I don't think we are distorting our institutional priorities or our commitment to what we perceive to be our academic mandate.

Mr. **Walgren**. Well, thank you very much for being a resource to us. We appreciate it and we look forward to continuing to have contact with you as this task force pulls together its report.

Dr. **Marks**. Thank you, I'd like that.

[Questions and answers for the record follow:]

RECEIVED
AUG 8 1986
COMMITTEE ON SCIENCE
AND TECHNOLOGY

Office of the President

July 28, 1986

The Honorable Don Fuqua
Chairman
Committee on Science and Technology
U.S. House of Representatives
Suite 2321
Rayburn House Office Building
Washington, D.C. 20515

Dear Mr. Fuqua:

Thank you for your letter of July 16, 1986 expressing your appreciation for my testimony before the Science Policy Task Force on April 23, 1986. As I indicated at that time, I know I share with a vast number of my colleagues in the science community our appreciation for the work that you and the members of the Congress are doing in evaluating our Nation's science policy.

You ask that I address certain follow-up questions in the sheet attached to your letter. I will try to do so as follows:

1. I do not believe that it is easy to adequately measure the outputs from biomedical research programs in terms of how the research investment benefits society in the immediate short term. There are clearly some examples of relatively short term payoff. In this area I would include the recombinant DNA products, such as insulin and human growth hormone which have reached the mark in a relatively short period of time from the inception of these important and powerful new technologies. These technologies are products of our research investment. Basically, however, the payoff from research is in its very nature, long term. What do I mean by long term? One can't be sure, but certainly a decade would be a reasonable time to try to measure payoff in terms of application. Among the criteria that could be used to quantify the payoff to society from research are:

    A. Disease prevention;

    B. Difinitive cures for diseases that previously were not amenable to effective treatment; and

    C. Expansion of the profitable product base of our pharmaceutical industry.

Memorial Sloan-Kettering Cancer Center
1275 York Avenue, New York, New York 10021

2. Strategies that are most likely to be effective in combating disease and improving health care are prevention of disease and maintenance of health. As an example, one can cite the decrease in the incidence of fatal coronary disease. While one can't precisely quantitate the factors that have contributed to this decrease, one can certainly include the evidence of the beneficial effects of certain dietary modifications, exercise and other measures that prevent arteriosclerosis.

   In the area of cancer, there is abundant evidence that perhaps the single most important factor that could decrease the incidence of cancer in this country would be a marked decrease in cigarette smoking, which is so closely associated with the continuing increase in the incidence of lung cancer. The effort to prevent lung cancer through a decrease in smoking probably would be facilitated if we could identify the population at risk. The presumption that there is a population at risk follows from the fact that many smoke and few get lung cancer. The strategies for identifying individuals at risk require a concerted continuing research effort. While increasing our commitment to research is the best hope for new strategies for prevention of disease, we must continue our commitment to support the best possible research which will lead to more effective therapies in the traditional approach to diseases.

3. The control of intellectual property should be such that its use is available and appropriately applied in the public interest. The largest fraction of basic researh in academic institutions is supported by public funds, primarily through the National Institute of Health and to a lesser extent the National Science Foundation. Intellectual property can most appropriately be controlled by the research institutions which created it and administered according to guidelines established through the Federal Government to assure their most expeditious and effective exploitation. Such exploitation should primarily occur in private sector. Appropriate incentives for the private sector to exploit new product opportunities are desirable but the ultimate control of the intellectual property should reside with the non-profit academic institutions if it is generated in such an institution.

4. Increase in industrial support for academic research is occurring in this country. I think that this has and can continue to occur without distorting of the important traditions of the academic institutions which have made biomedical research in the U.S. the most successful in the world. However, it does require constant attention to the guidelines for increased industrial academic relationships. In this regard, I have forwarded to Dr. Kiki Hellman a copy of the talk I recently gave dealing with concerns and recommendations with respect to increasing industrial support of academic research (attached). At the present time, it is estimated that about 6-7% of basic research in academic institu-

tions is supported by industry. The vast majority of this research is supported by Federal Government. Given these considerations, even if industrial support were to double, which is possible, the Federal Government will remain the primary source of support for basic research in academic institutions. This must mitigate against any reduction of Federal support of basic research while there is an increase in industrial support.

5. I am not sure that it is either necessary or desirable to develop some type of funding rewards system to benefit institutions that effectively and expeditiously transfer basic research findings to medical practice. The motivation for doing this, I think, is in place. All of us involved in biomedical research take great satisfaction in a product of our research which leads to an application that is useful in the prevention or treatment of disease or maintenance of health. This in itself is a major reward. On a more material level, effective application of a product of basic research generally involves, in this country, an industrial partner who will reward the academic institution and its scientists through either direct support of research, royalty income or even direct compensation. In other words I do not think that any additional reward system need be devised to stimulate the process further for fear that it will really distort our primary goals and priorities.

I trust the above will be of use to you in your further deliberations. Again, I express my appreciation and the opportunity of providing you with these comments.

Sincerely,

Paul A Marks

Paul A. Marks, M.D.

Mr. WALGREN. Let's turn, then, to Dr. Hiatt, who, as I said at the outset, is a professor of medicine at Harvard University and the associated hospital, Brigham and Women's Hospital in Boston.

Thank you for coming, Dr. Hiatt, and please proceed in whatever way you would like to make the point you feel ought to be stressed.

[A biographical sketch of Dr. Hiatt follows:]

DR. HOWARD H. HIATT

Dr. Howard Hiatt attended College and is a graduate of the Harvard Medical School. Trained in clinical medicine, biochemistry and molecular biology, he joined the faculty of the Harvard Medical School in 1955 as Director of the Cancer Research Laboratories at the Beth Israel Hospital. His research was directed at applying the concepts and technology of biological science to studies of the behavior of cancer cells and to the treatment of patients with cancer.

From 1963 to 1972, he served as Herman L. Blumgart Professor of Medicine at Harvard Medical School and Physician-in-Chief at Beth Israel Hospital. During that period, he and his colleagues developed teaching and research programs concerned with the application of biological science to our understanding of, and capacity to deal with, human disease in an environment in which the needs of patients as people were preeminent. Side-by-side with the focus on scientific advances in the Department of Medicine was an emphasis on outreach programs in the community.

From 1972 to 1984, Dr. Hiatt was Dean of the Harvard School of Public Health. There he worked with the faculty on programs in three general areas: disease prevention; strengthening the Nation's health care system; and international health. Several new programs involved bringing traditional public health experts together with scholars from a variety of other fields.

In 1984–1985 he was Visiting Scholar at the Institute of Medicine of the National Academy of Sciences, Washington, and at the King's Fund, London. In April and May he was Visiting Lecturer at the College de France, Paris.

Dr. Hiatt is the author of over 70 scientific papers and has written extensively for the lay press in areas of disease prevention and health services. In recent years, he has written and spoken about the health implications of the nuclear arms race.

In July, 1985 Dr. Hiatt returned to Harvard as Professor of Medicine at the Harvard Medical School and the Harvard School of Public Health. His office is now in the Department of Medicine, Brigham and Women's Hospital, where he is organizing a research training program in clincial effectiveness for young physicians.

Among the organizations of which Dr. Hiatt is a member are the Association of American Physicians, the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Society for Clinical Investigation. He has served as advisor to several U.S. Government and international committees concerned with health and scientific affairs.

STATEMENT OF DR. HOWARD M. HIATT, PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL AND THE HARVARD SCHOOL OF PUBLIC HEALTH, BRIGHAM AND WOMEN'S HOSPTIAL, BOSTON, MA

Dr. HIATT. Thank you, Mr. Walgren. I was, prior to my present position at Harvard, dean of the School of Public Health from 1972 to 1984, and for the decade before that, chief of the medical service at one of the Harvard Medical School teaching hospitals of Beth Israel in Boston and head of its Cancer Program.

I was asked today to speak primarily on biomedical research and its relationship to the public health and to programs of health care. I would like to focus primarily on five issues: the contributions of research to the public health; the importance of basic research; the importance of prevention in the control of disease; research and medical care; and the need for continuing support of the Nation's research enterprise.

The three leading causes of death in the United States and other industrialized countries are heart disease, cancer and stroke. This is in marked contrast to what prevails in the developing countries of the world, and what was true in the United States early in this century, when pneumonia and influenza, tuberculosis and infections of the gastrointestinal tract took the largest number of lives. They are diseases primarily of infants and children, and their control, then, meant a marked decrease in death rates among the young. Infant mortality in this country; that is, the number of babies that die in the first year of life for every 1,000 babies born. that number fell from over 100 at the turn of the century to something less than 11 at the present time. This means that more and more of our people are living to an age where they are candidates for the diseases that primarily afflict older people—heart disease, cancer and stroke. Pneumonia and influenza are now fifth on the list of killers in this country, and tuberculosis and gastroenteritis have long since disappeared from the list.

In no area of health, here or anywhere else, has progress been greater than in the prevention and the treatment of the infectious diseases such as, cholera, smallpox, plague, dysentery, diphtheria, tuberculosis, typhoid, typhus, and others that were scourges throughout the centuries. An outbreak of cholera in Hamburg, Germany, in 1892 produced 1,000 new cases a day, half of whom were to die. One 19th century epidemic in Cairo killed 13 percent of the inhabitants. The measures that proved most effective in the control of these diseases were those that come under the heading of public health technology: purification of the water supply, improved sewage disposal and other sanitary measures, improved personal hygiene, better nutrition, and less crowded living conditions. There was great progress, of course, as a result of vaccines and subsequently of antibiotics and other antibacterial drugs, but the public health measures achieved a great deal of control even in the absence of the newer forms of treatment.

Vaccines and the drugs often seem miraculous in their effects, but we sometimes lose sight of the fact that progress was extraordinary even before. Scarlet fever, which is caused by streptococcal infection, took the lives of 25,000 children per million children per year in Britain early in the 19th century. Deaths from streptococcal disease from scarlet fever began to fall in the early part of the 19th century, had fallen from 25,000 per year to 25 per year before the first antibiotic was found. That in no way denigrates penicilin. If a patient has a streptococcal infection, any doctor and any patient are extremely grateful to have the drug, and treatment is mandatory. Nonetheless, we shouldn't lose sight of the control that is achieved even in the absence of these drugs.

Similar events have occurred with other infections, including, for example, tuberculosis. Effective treatment of tuberculosis became available in the 1950's, but the mortality had begun to fall long before. In the 19th century in Europe, the death rate from tuberculosis dropped by more than a third before the cause of the disease was known, and deaths in the United States from tuberculosis decreased from 400 per 100,000 people per year to 30 before the first effective treatment was available. With the discovery of streptomycin and other drugs, tuberculosis is now almost completely controllable. However, again, it is useful to recall that considerable control took place before specific treatment was discovered. It is especially useful to think in those terms because there are parallels with some of today's primary disease problems.

With respect to the importance of basic research to health, the unfolding story of another infectious disease, AIDS, tells us a great deal. The advances in molecular biology and genetics of recent decades facilitated the discovery that a virus causes that disease. A particularly important lead was provided by studies of a virus that causes leukemia in cats. Much of the cat work was carried out in the 1970's before AIDS was even recognized. At that time questions were raised about the relevance of the cat research to human disease, and the scientists responsible could not have known then, or even now, of all benefits that their research would bring in terms of human health. They knew that they were asking important questions about the mechanisms of an important problem. The agencies that provided financial support knew that the work was of high quality. They could not predict, however, when and where any new discoveries might be useful.

As it turned out, the cat leukemia virus and the virus that causes AIDS are similar. Knowledge and methods obtained from the cat research helped identify the AIDS virus, and likely very much sooner than would otherwise have been the case. Although many obstacles to the development of a vaccine remain, isolating the AIDS virus will have been crucial. Clues that will lead to such a vaccine or to effective drugs against AIDS may come from the growing amount of research now going on in the AIDS field. But it may well come from seemingly unrelated basic research. Therefore, the AIDS story, like many others, tells us that we must encourage the search to extend the horizons of knowledge in the biomedical sciences. Among the most elegant examples of applied, or mission-oriented, research, with, as it turned out, profound basic knowledge fallout, was the work of Louis Pasteur, who set out to learn how to prevent wine from turning to vinegar. That was the purpose. In the process, he discovered bacteria and started the science that established the relationship of germs of disease.

However, premature diversion of resources from basic research to applied can be harmful to the very problem that one is attempting to solve. An example from the cancer field strengthens this point. One of the few truly new effective anticancer drugs since the beginning of the war on cancer in the early 1970's is cisplatin. That drug was discovered by a physicist, Barnett Rosenberg, who was interested in the effects of electrical currents on cell division in bacteria. He had made some observations and read of others on this subject, and working in a department of biophysics with, I suspect, the problem of cancer remote from his mind, he found that bacteria were in fact inhibited from dividing when he turned the current on. As it turned out, the inhibition was not the result of the current itself. Rather he had been generating current with platinum electrodes, and the platinum had undergone a slight degree of decomposition. The products of the decomposed platinum included cisplatin, a seemingly new compound which interfered with the cells reproducing themselves. This "new" compound, he subsequently learned, had first been made in 1845. He pursued his observations and found that cisplatin inhibited not only bacteria, but animal cells as well. This, in turn, led to a series of tests against cancer in animals and finally against human cancer. Cisplatin proved to be effective against several forms of cancer in people. It was discovered by a scientist who was not doing cancer research. Had the funds that made his first work possible been directed toward a search for anticancer drugs and away from the basic research he was doing, cisplatin would likely not be among the drugs now available for cancer chemotherapy.

As I mentioned earlier, the experience that we had with infectious diseases in the 19th and the early 20th centuries, so with cancer, heart disease and others of today's major killers: prevention is generally far more effective than treatment. Cures of cancer as a result of modern chemotherapy treatment programs represent milestones in medical progress. The cures are the more notable for the principal beneficiaries of the young, the young who suffer particularly from acute leukemia, from Hodgkin's disease and other forms of lymphoma. More than 3,000 cancer victims under the age of 30 years are saved each year. A larger number of older people with cancer are also cured with drugs. Experts in the cancer field debate what chemotherapy could do for other forms of cancer, but a realistic assessment suggests that until we know a lot more about that disease, it is unlikely that the total number of patients cured by chemotherapy will exceed 30,000 and perhaps considerably fewer. Even that would be a remarkable achievement, but recall that more than 460,000 Americans died of cancer in 1985. Thus, the number of potential cures is low in terms of the size of the overall cancer problem. It is also small relative to the more than 150,000 persons who die each year of smoking-related, and therefore, clearly preventable cancers, particularly lung cancer.

If lung cancer deaths were occurring now at the same rate as in 1930, the annual deaths from that cause would be less than 10,000. The difference from what is expected this year, something of the order of 126,000, doesn't indicate that medical treatment is less effective, of course. Rather it reflects what is really an epidemic of the disease as a result of cigarette smoking. Cancer of the lung now strikes more than 10 times as many Americans as it did 55 years ago. Treatment programs now cure fewer than 10 percent of people with lung cancer. As a result, in the past half century, lung cancer has moved to first on the list of cancer killers by a wide margin. It now kills more Americans than the next three most common causes of cancer combined.

In sharp contrast, stomach cancer, which was first on the list of fatal cancers 50 years ago, has been steadily decreasing over the years to a position of seventh on the list at the present time. It is still an important problem: it claimed more than 14,000 lives last year. But if it were occurring at the same rate as in 1930, it would now be causing more than 75,000 deaths a year. In other words, more than people who would have died from stomach cancer had the prevalence of the disease continued as it was, are "saved." As is true of lung cancer, the change is unrelated to medical programs. If you are unfortunate enough to get stomach cancer in 1986, your chances are being saved of the disease are of the order of 10 percent, about what they were 20, 30, or 40 years ago. Treatment is about as successful as treatment of lung cancer. The marked drop in stomach cancer deaths comes not from medical intervention, but from some change in an environmental factor or factors that were responsible and are responsible for the disease. We know what is responsible for the increase in lung cancer. We can only guess what is responsible for the decrease in stomach cancer.

In this day of great concern with the cost of medical care, it is important to keep in mind that research can bring not only the control of disease, but also a reduction in cost. This is true of several vaccines against common childhood diseases. The use of a vaccine to prevent measles, for example, has been shown to save more than five times its cost. I am not suggesting that most biomedical research or most preventive programs lead to the saving of money. They don't, but their goals are to save lives and to improve the quality of life, not to save money. We don't ask when we use penicillin to treat a child with scarlet fever, whether we are saving money. It seems to me no more logical to ask that question when we prevent disease in our population.

The mention of health care costs leads me to turn briefly to consider research in health services. This kind of research involves not biological, but statistical and epidemiologic approaches. It asks such questions as, will that additional CT scan increase the prospect of a better outcome for the patient with a headache? Will this patient with heart disease do as well with medication as with a coronary bypass operation? It has been estimated that we waste many billions of dollars each year on unnecessary procedures of many kinds, while subjecting patients to unnecessary risks and suffering. Health services research has not gotten much attention from Government agencies or from the academic community until recently. It needs to be encouraged.

Such research requires statisticians, epidemiologists, economists, and other social scientists to work with physicians. For example, cardiologists are working with a group of social scientists now to sort out the factors responsible for the more than 30 percent fall in deaths from coronary artery disease in the past 15 years. This has been one of the most extraordinary phenomena of our time. Deaths from heart disease began to fall in the United States some time in the mid-sixties, and that has continued up to the present time. The explanation is in part some of the new approaches we have to the management of people with heart disease: coronary care units, cardiac surgery, new drugs. But that explains only a very small part of the phenomenon. After all, these same advances are seen in many of the European countries where there has been no fall in deaths from heart disease. The best explanation for this extraordinary phenomenon is, more likely, change in diet, change in exercise patterns, better treatment of hypertension, and particularly, change in smoking habits. But we are not absolutely sure, and it is crucial that we find out so that when the responsible causes are better identified, those leads can be pursued.

Research differently motivated and based to a considerable extent on engineering and the social sciences designed to rehabilitate and to make life more comfortable is required to help people with illnesses that cannot be cured or prevented. The number of people with such needs is increasing as our population grows older. Included are people with chronic illnesses, both physical and mental, and the mentally handicapped. Their needs range from better methods of pain relief to better technology to compensate for difficulties in hearing, vision and locomotion, to better ways to live alone when necessary or desired.

Now, despite the great strides that have been made in the control of today's health problems, we have seen only the barest beginnings of the job. The gaps are still very great in our understanding of virtually all of today's major diseases; ways to treat more effectively or to prevent cancer; the complications atherosclerosis, such as heart attacks and stroke; arthritis; emotional and mental diseases; mental deficiency; the diseases of aging; the neurological diseases—the list can be greatly lengthened. Solutions don't merely await the assembling of the pieces of a set of puzzles. Far more pieces are missing than those that have been uncovered. Many that are missing will turn up in unexpected and unlikely places.

To accelerate the appearance of missing pieces, it is important to encourage the ablest people who are motivated and qualified to carry out basic research to pursue their interests and to help make it possible for them to do so. Fortunately, we are in a strong position to continue the basic research that is so necessary to the challenges before us, thanks in large part to the research enterprise built principally with enlightened Federal support in the years following World War II. Scientists now have insights into many fundamental areas that were mysteries just a few years ago. Most have emerged as a result of basic research, and many with NIH support. These insights permit more informed questions about the serious diseases that surround us.

However important the continuation of strong efforts in basic and applied biomedical research, they are clearly not sufficient to deal adequately with many of the health problems that confront the Nation today. Again, the AIDS problem is an example. We can do a great deal toward preventing that disease, even without the vaccine we are hoping that will be developed, and without the drugs that could be so important. What is also needed, then, is research in the social sciences relevant to that problem, and relevant to a variety of other health problems including, of course, the problem of smoking.

Limitations in our capacity to deal with most of today's most serious diseases constitute a compelling reasons to preserve and extend the biomedical research enterprise we now have and to strengthen our public health-oriented sciences capabilities. The fragility of that enterprise was hinted at when one of the most authoritative journals in Britain, "Nature," a short time ago expressed the editorial view that the British biomedical research enterprise, which was not so long go comparable in many ways to our own, is now on its last leg. This is considered by many British scientists not to be overstatement. One of the most distinguished scientists in Britain, Sir Hans Kornberg, ascribes this in part to shrinkage of government support and that, in turn, to public disenchantment with science, with the realization that basic research does not immediately lead to economic benefit.

The British experience is one that I think has lessons of great importance for us. Thank you, Mr. Chairman.

[The prepared statement of Dr. Hiatt follows:]

Testimony before the Committee on Science and Technology

Howard H. Hiatt

April 23, 1986

Mr. Chairman and distinguished Members of the House of Representatives:

It is an honor for me to have the opportunity to testify before you. I have been asked to comment on the contributions of biomedical research to the public health and to programs of health care. I am pleased to do so and will focus on five principal issues:

1. The contributions of research to the public health;
2. The importance of basic research;
3. The importance of prevention in the control of disease;
4. Research and medical care; and
5. The need for continuing support of the nation's research enterprise.

The three leading causes of death in the United States and other industrialized countries are heart disease, cancer and stroke. These are mainly diseases of older people. In contrast, at the turn of the century the three leading killers were conditions caused by infections with bacteria or viruses: pneumonia and influenza, tuberculosis, and gastro-intestinal infections. Because they affected mainly infants and children, their control meant a marked decrease in death rates among the young. Infant mortality, that is, the number of babies dying in the first year of life per 1000 live births fell from more than 100 in 1900 to 11 at present. That, in turn, has meant that more and more people live to an age at which they are candidates for heart attacks, cancer and stroke. Pneumonia and influenza have fallen to fifth among the major causes of death, and tuberculosis and gastroenteritis have long since disappeared from the list.

In no area of health has progress been greater than in the prevention and treatment of contagious diseases. Cholera, smallpox, plague, dysentery, diphtheria, tuberculosis, typhoid, typhus and others were scourges through the centuries. An outbreak of cholera in Hamburg, Germany in 1892 produced 1000 new cases a day, one-half of whom were to die. One nineteenth century epidemic in Cairo killed 13% of the inhabitants. The measures that proved most effective in the control of these diseases were those that come under the heading of public health technology--purification of the water supply, improved sewage disposal and other sanitary measures, improved personal hygiene, better nutrition and less crowded living conditions. Further progress occurred as a result of research that led to vaccines that are effective in preventing many of these diseases, and the many drugs that are active against infections caused by bacteria and some viruses.

The effects of the vaccines and drugs often seem miraculous. However, we must not lose sight of the often even greater contributions of non-medical measures to the control of the infectious diseases. For example, in the early nineteenth century deaths from streptococcal disease among English children occurred at a rate of 25,000 per million children per year. Over the next hundred years, and before the first antibiotic was discovered, that figure fell to 25 per million children per year. This in no way denigrates the effects of the antibiotics: in patients with streptococcal infections, penicillin can be life-saving. However, a variety of other measures--improved nutrition, better personal hygiene, and other factors still unidentified-- played a crucial role in much of the control of this and many other bacterial and viral diseases.

Similar stories can be told about other infectious diseases, for example, tuberculosis. Effective treatment of tuberculosis became available in the 1950s, but the mortality had begun to fall long before. Indeed, in the nineteenth century in Europe the death rate from tuberculosis dropped by more than a third even before the cause of the disease was known. Deaths in the United States from tuberculosis decreased from 400 per 100,000 people per year to 30 before the first effective treatment was available. With the discovery of streptomycin and other drugs, tuberculosis became almost completely controllable. However, it is important to recall that considerable control took place before specific treatment was discovered.

The unfolding story of the acquired immune deficiency syndrome (AIDS) epidemic illustrates in several ways the importance of basic research to health. The advances in molecular biology and genetics of recent decades facilitated the discovery that a virus causes the disease. A particularly important lead was provided by studies of a virus that causes leukemia in cats. Much of the cat work was carried out in the 1970's, before AIDS was even recognized. The scientists responsible could not have known then (or even now) of all the benefits their research would bring in terms of human health. They knew they were asking important questions about the mechanisms of an important problem. The agencies that provided financial support knew that the work was of high quality. They could not predict, however, where and when any new discoveries might be useful.

As it turned out, the cat leukemia virus and the virus that causes AIDS are similar. Knowledge and methods obtained from the cat research helped identify the AIDS virus and likely much sooner than would otherwise have been the case.

Although many obstacles to the development of a vaccine remain, isolating the AIDS virus will have been crucial. Clues that will lead to such a vaccine or to effective drugs against AIDS may come from the growing amount of research now going on in the AIDS field. But it may well come from seemingly unrelated basic research. Therefore, the AIDS story, like many others, tells us that we must encourage the search to extend the horizons of knowledge in the biomedical sciences.

Among the most elegant examples of applied, or mission-oriented, research (with, as it turned out, profound basic knowledge fall-out), was the work of Louis Pasteur, when he set out to learn how to prevent wine from turning to vinegar. In the process he discovered bacteria and started the science that established the relationship of germs to disease.

But premature diversion of resources from basic research to applied can be harmful to the very problem that one is attempting to solve. An example from the cancer field strengthens this point. One of the few truly new effective anticancer drugs since the beginning of the war on cancer is Cisplatin. The drug was discovered by Barnett Rosenberg, a physicist who was interested in the effects of electrical currents on cell division in bacteria. Working in a department of biophysics--not connected to any unit concerned with cancer, or even with any other aspect of health--he found that bacteria were inhibited from dividing when he turned the current on. As it turned out, the inhibition was not the result of the current itself. Rather, he had been generating current with platinum electrodes, and the platinum had undergone a slight degree of decomposition. The products of the decomposed platinum included Cisplatin, a seemingly new compound, which interfered with the cells reproducing themselves. (The "new" compound, the physicist subsequently learned, had first been made in 1845.) Pursuing his observations, he found that Cisplatin inhibited not only bacteria, but animal cells, as well. This, in turn, led to a series of tests against cancers in animals, and finally against human cancer. Cisplatin proved to be effective against several forms of cancer in people. It was discovered by a scientist who was not doing cancer research. Had the funds that made his first work possible been directed towards a search for anticancer drugs and away from the basic research he was doing, Cisplatin would likely not be among the drugs now available for cancer chemotherapy.

As is true of the infectious diseases, so with cancer, heart disease, and other of today's major killers: prevention is a far more effective approach than treatment. Cures of cancer as a result of modern chemotherapy treatment programs represent major milestones in medical progress. The cures are the more notable, for the principal beneficiaries are the young: more than 3000 cancer victims under the age of 30 years, are saved every year. A larger number of older people with cancer are also cured with drugs. Experts in the cancer field debate what chemotherapy could do for other forms of cancer. But a realistic assessment suggests that until we know a lot more about cancer, it is unlikely that the total number of patients cured by chemotherapy will exceed 30,000 per year. That would be a remarkable achievement, but more than 460,000 Americans died of cancer in 1985. Thus, the number of potential cures is low in terms of the size of the overall cancer problem. It is also small relative to the more than 150,000 persons who die each year of smoking-related, and therefore, preventable cancers, particularly lung cancer.

If lung cancer deaths were occurring at the same rate now as in 1930, annual deaths from that cause would be less than 10,000. The difference, that is, an increase of more than 116,000 deaths per year from lung cancer, does not indicate less effective medical treatment. Rather, it reflects what is really an epidemic of the disease as a result of cigarette smoking. Cancer of the lung now strikes more than ten times as many Americans as it did 55 years ago. Treatment programs cure less than 10% of people with lung cancer. As a result, in the past half century lung cancer has moved to first on the list of cancer killers by a wide margin--it now takes more lives than the next three most common causes of cancer deaths combined.

In sharp contrast, stomach cancer, which was first on the list of fatal cancers 55 years ago, has been steadily decreasing over the years, to a position of 7th at the present time. It is still an important problem: it claimed more than 14,000 lives in 1985. But if it were occurring at the same rate as in 1930, it would now be causing more than 75,000 deaths a year. In other words, more than 60,000 people are "saved" annually from stomach cancer deaths. As is true of lung cancer, the change is unrelated to medical programs. Indeed, like lung cancer, cancer of the stomach continues to be among the most resistant to treatment. Fifty years ago, of those who got stomach or lung cancer, fewer than 10% could be cured. Treatment results today are only slightly better; about 15% of stomach cancer and 10% of lung cancer victims are cured. Thus, it can only have been changes in environmental factors that led to a marked drop in stomach cancer deaths. In other words, we can credit environmental changes with the saving of more then 60,000 lives per year from that disease.

We know what is responsible for the increase in lung cancer. We have only guesses as to what has caused the decrease in stomach cancer. (One guess is that refrigeration and preservatives have decreased the presence in foods of cancer-causing toxins, which, the theory goes, are made by contaminating organisms.) But we can say with confidence that medical treatment can neither be credited for the marked decrease in deaths from one, nor faulted for the even more marked increase in deaths from the other. We can, however also say that whatever the factors responsible for the decline in stomach cancer, they have decreased the immediate need for medical services, just as cigarettes have been increasing the need.

In this day of great concern with the costs of medical care, it is important to keep in mind that research can bring not only the control of disease, but also a reduction in costs. This is true of several vaccines against common childhood diseases; the use of vaccine to prevent measles, for example, has been shown to save more than five times its cost. I am not suggesting that most biomedical research leads to the saving of money; it does not. But its goal is to save life and to improve the quality of life, not to save money.

The mention of health care costs leads me to turn briefly to consider research in health services. This kind of research involves not biological, but statistical and epidemiologic approaches. It asks such questions as, will the additional CT scan increases the prospect of a better outcome for that patient with a headache? or, Will this patient with heart disease do as well with medications as with a coronary bypass operation? We are wasting billions of dollars each year on unnecessary procedures of many kinds, while subjecting patients to unnecessary risks and suffering. Health services research has not gotten much attention from government agencies or from the academic community until recently. It needs to be encouraged.

Such research requires statisticians, economists and other social scientists to work with physicians. For example, cardiologists are working with statisticians and epidemiologists to sort out the factors responsible for the more than 30% fall in deaths from coronary artery disease in the past 15 years. Treatment programs have contributed to the improvement, but their role is less important than that of other factors, such as changes in smoking habits, diet, and exercise. More precise information could provide guidance to decisionmakers obliged to divide scarce funds. Decisions about how much should be put, for example, into epidemiologic research, how much into new coronary care facilities, and how much into attempting to extend the various preventive measures that can be shown to play a role require objective data. Other questions relating to the allocation of scarce health resources would also benefit greatly from more interdisciplinary research of this sort.

Research differently motivated and based to a considerable extent on engineering and the social sciences--designed to rehabilitate and to make life more comfortable--is required to help people with illnesses that cannot be cured or prevented. The number of people with such needs is increasing as our population grows older. Included are people with chronic illnesses, both physical and mental, and the mentally handicapped. Their needs range from better methods of pain relief, to better technology to compensate for difficulties in hearing, vision and locomotion, to better ways to live alone when necessary or desired.

Despite the great strides that have been made in the control of today's health problems, we have seen only the barest beginning of the job. The gaps are still very great in our understanding of virtually all of today's major diseases. Ways to treat more effectively or to prevent cancer, the complications of atherosclerosis, such as coronary heart disease and stroke, arthritis, emotional and mental diseases, mental deficiency, the many infirmities of aging, the neurological diseases--the list could be greatly lengthened, of course--do not merely await the assembling of the pieces of a set of puzzles. Far more pieces are missing than those that have been uncovered. Many that are missing will turn up in unexpected and unlikely places.

To accelerate the appearance of missing pieces, it is important to encourage the ablest people who are motivated and qualified to carry out basic research to pursue their interests and to help make it possible for them to do so. Fortunately, we are in a strong position to continue the basic research that is so necessary to the challenges before us, thanks in large part to the research enterprise built principally with enlightened federal support in the years following World War II. Scientists now have insights into many fundamental areas that were mysteries just a few years ago. Most have emerged as a result of basic research, and many with NIH support. These insights permit more informed questions about the serious diseases that surround us.

However important the continuation of a strong effort in basic and applied biomedical research, it is clearly not sufficient to deal adequately with many of the health problems that confront the nation today. Control of the AIDS epidemic cannot await the development of vaccines and effective drugs. It is urgent that we use existing methods of prevention, while seeking new ones. We know that the principal methods of AIDS transmission are rectal intercourse among homosexual men and the use of contaminated syringes or needles by people taking intravenous drugs. The danger of AIDS transmission appears to have led to behavioral changes in some people. However, the limited success of this kind of health education is one more reflection of the need for rigorous programs of research in the social and behavioral sciences.

The diseases caused or aggravated by smoking are another obvious focus for considering the potential health benefits of more research in the social sciences. Many smokers are physically addicted to tobacco. Therefore, the biology of addiction is one important avenue for research on tobacco and health. But that doesn't tell us what effective measures might be taken to prevent children from beginning the habit, and thereby from becoming addicted.

Research in the social and behavioral sciences is also important for clinically useful information on many other of today's major threats to health. For example, success has been limited in persuading people who have high blood pressure but who feel well that it is in their interest to take medication every day. Consider also how poorly we now deal with such other major health problems as many kinds of accidents, alcohol abuse, and drug addiction.

Limitations in our capacity to deal with most of today's most serious diseases constitute a compelling reasons to preserve and extend the biomedical research enterprise we now have and to strengthen our public health-oriented sciences capabilities. The fragility of such activities is hinted at when we read in the most authoritative scientific journal of the United Kingdom the editorial view that the British biomedical research enterprise, not so long ago comparable to our own, "is on its last leg". One of Britain's most distinguished scientists ascribes in part the shrinkage of government support that is partly responsible to a "public disenchantment with science and the realization that basic support does not immediately lead to economic benefit".

The British experience offers a sober lesson.

DISCUSSION

Mr. **Walgren**. Well, thank you very much, Dr. Hiatt. There is obviously so much to be done. Is there anything you would like to add about how to allocate resources between prevention and treatment? You are clear in your testimony that if you don't know what the mechanisms are, you clearly can't make any judgment in that area, but that the preventive efforts have clearly yielded such large numbers of lives helped that our attention should certainly go in that direction.

Dr. **Hiatt**. The effort that we have made to explain the cause of disease and understand its mechanisms, and then to control it with treatment, those efforts have paid off handsomely, and certainly should be continued. I know we have done much less for the sciences that are important for prevention, Epidemiology statistics and now the newer decision sciences, I think, are important to support in their own right. I think it is important to support the kind of training in those fields for physicians, as well as nonphysicians. We have had a remarkable demonstration in the last three decades of how important the education of physicians in the biomedical sciences can be.

A large part of the academic strength in this country now is the result of efforts in that direction promoted by the National Institutes of Health and by private agencies, but particularly the Government through the NIH. The career pattern for many people in academic medicine at the present time has been following clinical training 2 or 3 years in a biochemistry or a molecular biology setting, followed by work related to disease.

We haven't seen the same phenomenon encouraging people to get some background in the epidemiologic, the statistical sciences. And as a result, I think we find ourselves not able to make the same judgments in that area of medicine that we have been able to make understanding the basis of disease.

Mr. **Walgren**. Why is that that they haven't been that interested? I gather the medical schools don't emphasize it in ways that perhaps could be, and people are preoccupied in going elsewhere?

Dr. **Hiatt**. Well, I think that the revolution in biology has been so extraordinary, the opportunity to learn the mechanisms of disease, the importance of applying what has happened in the biological sciences to medicine—all has been exploited very handsomely. I think all of us in academic medicine have been rather slower to appreciate how much there was, and is, to be learned from applying the epidemiologic approaches to disease.

Mr. **Walgren**. At bottom, those things are really behavioral—well, I don't know that they are behavioral, but I gather what you are interested in studying in a statistical review is whether or not some kinds of behavior often pops out at you and indicates that it is leading to a detrimental result. And yet the behavioral sciences have just been literally ignored by at least much of our Federal Establishment. Certainly that is true in the National Science Foundation, at least percentagewise. I don't know that much about NIH's balance in that area, but to what should we ascribe the literally turning our back and walking away from behavioral and social sciences in this country?

Dr. **Hiatt**. I think perhaps in part it is the state of the sciences. They are in a much earlier state and less precise, and it is much more difficult, I think, to readily find areas that can be applied.

Mr. **Walgren**. They are inherently less demonstrable, as well. If you are talking about changing a percentage of 1,000 events, that is very different than being able to show that 100 percent of a certain kind of molecule, when stimulated a certain way, reacts and combines and produces a certain product, and so they are more difficult to appreciate because you have to actually sit down and contemplate an abstract thought rather than see a physical product, I gather.

Dr. **Hiatt**. Well, I think that the outcome that you look for is much more delayed. It is much less precise, as you say.

There are two aspects in the area of prevention. One, of course, is establishing cause and effect. That generally requires long-term research. Once cause and effect relationships have been identified, as is true, let's say, of cigarettes and lung cancer or cigarettes and heart disease, then the problem of changing human behavior comes to the fore, as you indicate. Our capacity to deal with that is still very limited.

I think that there is the risk, because of its difficulties that we turn our backs on it. It has not attracted as many people as the biological sciences, and there has been a cut in NSF's support of the behavioral sciences in the last few years. I think it is shortsighted. In the long term, it is not in our interest to turn our back on that area.

Mr. **Walgren**. Any suggestions as to how to increase the appreciation of the kinds of statistical and epidemiological investigations that would hold potential if they were carried out?

Dr. **Hiatt**. I think more support for some of the public health sciences like epidemiology and biostatistics, more support for research in that area would be useful. I think more support for training in those areas for physicians, more support for work that looks at the outcome of interventions.

We know, for example, that coronary bypass surgery is an extremely important addition to our capacity to deal with coronary heart disease. On the other hand, it is apparent from studies that have been carried out, that we are doing coronary bypass surgery in a substantial fraction of patients for whom medical measures would be just as effective. But the number of people in clinical departments who are equipped to pursue such questions to set up studies of that sort is limited. Further, that kind of research particularly clinical trials, is expensive.

That is complicated by the fact that immediate beneficiaries are not readily identifiable. The insurance companies, the private sector, Federal agencies like Medicare, the individual, all who pay for these procedures. As a result, it's not always clear where the responsibility rests for the research that might tell us how many procedures are necessary and how many are not.

The beneficiaries, ultimately, of course, are the American people, and I think it is important that the Health Care Financing Administration, which pays for so much care directed at the diseases of older people—heart disease, cancer and stroke, support more research that will permit us to know how many of our interventions are useful and how many are less so.

Mr. WALGREN. Let me recognize Chairman Fuqua.

Mr. FUQUA. Thank you, Dr. Hiatt. I just have a couple of questions. You mentioned in your testimony about the refrigeration and preservatives have decreased the present cancer-causing toxins. Has that been recently, or has that been over a long period of time when refrigeration came into being. It has been around--modern refrigeration—since the end of World War II.

Dr. HIATT. In this country the fall in stomach cancer began 30 or 40 years ago. It has progressed up to the present time. Japan, which has the highest incidence of stomach cancer in the world, has only recently begun to show some fall. The cause is not known. One suggestion concerns food preservation, but that idea is very soft. It is possible, as you imply, that refrigeration that we have known with food now for 30 or 40 years has played a role.

Mr. FUQUA. That was, I guess, really the question, how long has that been, whether it has been more recent or had it been over a longer period of time, and you have answered that.

One other question, how much or what balance should there be between Government-directed research or congressional-directed research, and nondirected or targeted research, and how can we better arrive at a balance between those two if there should be a balance and who should be involved in trying to make those decisions?

Dr. HIATT. The answer to that question is one that would be presumptuous of me to offer. I think that it is crucial, given the very limited understanding that we have of most of the major health problems that confront us at the present time. I think it would be shortsighted to attempt to put too much emphasis on applied research, too much emphasis on disease-oriented research unless, as is the case now at the NIH, a large fraction of the so-called disease-oriented research Institutes recognize that support of basic research is essential.

The advances, for example, in the last decade and a half in our understanding of cancer have come not as a result of scientists setting out to cure cancer by, let's say looking for a drug. Rather, it has been scientists who have been encouraged to pursue questions of interest to them; questions that look as though they are ready to be pursued.

It is said that one of the important aspects of doing good science is to know when to ask a question as well as to know what question to ask.

Mr. FUQUA. I guess what I am saying is that you have been around a while also. Congress directed that there be a National Institute of Cancer, a National Institute of Heart, Stroke and others in NIH, and we have moved in in other areas—not necessarily biomedical research. This committee moved in several years ago to put in an infusion of funds into the National Science Foundation for these supercomputers. Periodically, Congress, responding to needs as they perceive them, has moved in those directions. Now, when the Institute was created within NIH, they were resisted by the professionals at NIH probably for good reason. Congress felt that this was necessary to do that. That is the type of thing I am speaking of.

We had very excellent testimony yesterday that, in fact, said it is fine if you do that as long as you don't tell us how to conduct and manage the research within that, and I am not referring to that, but I am referring to the broad areas. Is it bad for the public policy for the Congress or the Government—and sometimes the administration has proposed initiatives in certain areas—is it bad public policy for the Government to get involved and say these are areas that we think, Mr. NIH, that you should put further emphasis on, or the biomedical community, or other facets of the Government, because we think they are very important? It could be recombinant DNA research. Is that good or bad, or is there a balance, or do we do too much? Do we interfere in doing that?

Dr. HIATT. My view is that the support for the research comes from the American people. The Congress represents the American people, and as such, it is crucial that there be the kind of input that exists at the present time. I think, for example, there must be mechanisms to ensure that a problem like AIDS gets the attention of the scientific community that it deserves.

Mr. FUQUA. A case where Congress put additional funds into that last year.

Dr. HIATT. That, I think, was crucial. My own view is that we would serve ourselves better if we gave some greater latitude to the people at the NIH, particularly to the people without specific institutional affiliation. Dr. Fredrickson is here today, and the former director of NIH is in a position to speak to this. I haven't spoken to him about it, but it seems to me that the NIH approach could be greatly strengthened if a larger fraction of the resources available were put in the hands of a group that could take an overview and could say that at this time, perhaps more money for heart disease or more money for arthritis or more money for diabetes makes less sense or makes more sense, and where that same kind of detachment might be used in determining what fraction of the total research budget goes into basic research.

I think that of major importance is the preservation of that element called basic research, how we can preserve it, how we can extend it. I am sure there are a variety of ways, but certainly the input of the Congress in this issue is extremely important.

Mr. FUQUA. Thank you. Thank you, Mr. Chairman.

Mr. WALGREN. Let me ask just one question on this targeting business. You give the example of Pasteur pursuing wine, and that in a sense we say, "Look, we know all about that that has come out of the most inadvertently buildup of a knowledge base." Is there some way that we could estimate the drive on progress from where apparent serendipity—that word that means lucky inadvertent discovery versus targeted pursuit? This is along the lines that the chairman asked. So we want the money into cancer. Well, we might find the cure to cancer by flying a kite with an electrical hangup, but chances are less. Is there any way that we can estimate the value of targeting as opposed to nontargeting?

Dr. HIATT. I don't know. I do think that, as Dr. Marks said, identifying the best people, giving them the wherewithal to ask the questions that seem to them to be most interesting and most likely to yields answers is essential. The presence of some oversight structure with people identifying the problems that are most important to the Nation, health problems, and the ripeness of an area for application, I think that, too, is important.

Mr. **Walgren**. Well, thank you very much on behalf of the committee. We appreciate it, and we will look forward to being in contact with you as we develop this. Thanks very much for your time.

The time has somewhat gotten away from us, and we have invaded the time available for the rest of the witnesses, and have to somehow, or the other, encourage you to really be briefer in your presentation; not that we didn't want to do it the other way, first, but we are going to run into commitments during the noon hour, and that is going to make things not so great. So let's turn to Dr. Greene at this point, who, as you know, is the Director of the Medical Research Service of the Veterans' Administration. If I could impose on you and ask you to somehow, or other, just pursue what you can pursue with us in 10 minutes or so, and that will leave a little time for us to develop a dialog, and then we can pursue it in more detail with these three witnesses perhaps after the hearing as this report is developed.

I want to apologize for not having balanced the time more evenly among all our witnesses this morning. It is not an expression of diminished appreciation for your coming. So, Dr. Greene, go ahead and tell us what you think ought to be emphasized for a report like this that we are trying to put together.

STATEMENT OF DR. RICHARD J. GREENE, DIRECTOR, MEDICAL RESEARCH SERVICE, DEPARTMENT OF MEDICINE AND SURGERY, VETERANS' ADMINISTRATION, WASHINGTON, DC

Dr. **Greene**. Thank you, Mr. Walgren. I am very pleased to have this opportunity to describe VA's medical research effort. VA's support of biomedical research is supported with an annual budget of approximately $100 million. That includes investigation in virtually all areas of biology and medicine. The research is carried out principally by physician scientists, and I emphasize this, who work in VA medical centers as both researchers and clinicians. VA scientists hold academic appointments at medical schools and universities affiliated with VA medical centers, and funding for individual studies is based on rigorous peer scientific review by standing committees composed primarily of non-VA academic scientists.

At the outset I wanted to emphasize three things that distinguish the VA's efforts in biomedical research from other such efforts. First is that the VA's biomedical research program is closely linked to the agency's patient care mission. To this end we principally support and train physician investigators who pursue research part time while spending the majority of their time caring for patients in VA hospitals. About 75 percent of the 2,500 VA-supported principal investigators are physicians.

The second point I want to emphasize is that the VA's research program is intentionally oriented toward clinical investigation. While we do support a significant amount of basic biological research, the average investigator in our system is studying the cause and/or the treatment of a disease prevalent among VA patients.

And, third, the VA's biomedical research program is intramural. We support VA scientists who carry out their studies in VA medical centers. We do not make grants or contracts to private institutions. Our major objective of the VA's research effort is to establish a spirit of scientific inquiry in VA medical centers that enhances the quality of patient care.

I would like now to give a brief description of the four major programs that make up our research portfolio.

The largest of these which accounts for 75 percent of our research effort, is the Merit Review Program, where our funds are expended to support projects conceptualized, planned, and implemented by scientists at VA medical centers. Proposals to undertake such studies are developed at the local level, reviewed at the medical center by the R&D committee and appropriate subcommittees on human and animal subjects. Once approved at the local level, the proposal can then be submitted to the Medical Research Service in VA's Central Office where it is rigorously peer reviewed by our Merit Review Program. The scientific evaluation of research proposals is carried out by 14 standing merit review committees organized by medical discipline and composed of national experts drawn primarily from academic medical centers. The merit review system is organized in this manner to assure that we support only meritorious scientific studies.

The investment of such a large portion of resources in the Merit Review Program reflects our conviction that science and medicine are most likely to advance in a system that, one, allows scientists themselves to chose the problems that they wish to study; and, two, supports those proposed research projects that peer experts believe are most meritorious. And I think this reflects perhaps some of the questions that were asked of the previous witnesses, and we would agree completely that the way to expend research resources that are scarce is to support those people who have the best ideas. In other words to focus on investigator initiated ideas most heavily. In the VA this philosophy results in the support of 2,000 investigators who work in virtually all areas of biology, medicine, psychiatry, and surgery. VA scientists supported by the Merit Review Program are exploring the pathological processes that result in such diseases as diabetes, Alzheimer's disease, schizophrenia, alcoholism, and cancer. Other VA laboratories are attempting to develop new and effective therapies for spinal cord injury, heart disease, psychoses, and AIDS, to mention but a few examples.

I will describe now the Cooperative Studies Program which supports large-scale multihospital clinical trials that evaluate promising new medical and surgical therapies. Because the VA's research program is intimately linked to its patient care effort, significant economies are achieved by carrying out control trials in the VA medical care setting. In evaluating the relative effectiveness of alternative treatments, data must be pooled from large numbers of patients who are treated with an identical protocol. Such studies can efficiently be performed in the VA medical care system utilizing the expertise in research design and statistical methodology that has been developed in our Cooperative Studies Program.

The VA has carried out some landmark clinical trials that established effective therapies for tuberculosis, psychoses, and hypertension. Examples of current VA cooperative studies include evaluation of drugs for the treatment of epilepsy, heart disease and hypertension in the elderly, and the evaluation of new surgical techniques for the treatment of laryngeal cancer and lower limb vascular occlusions.

It is especially rewarding when a basic scientific discovery results in a new therapy that proves effective in a carefully controlled clinical trial. The VA is about to launch a cooperative study on the effectiveness in prostate cancer treatment of a new compound developed by one of our outstanding basic scientists, Dr. Andrew Schally of the New Orleans VA Medical Center. Dr. Schally's basic research studies on how hormones of the hypothalamus of the brain control endocrine gland function resulted in his receiving the 1977 Nobel Prize in Medicine. Recently, Dr. Schally has turned his attention to the development of a series of synthetic chemical compounds that differ slightly from natural brain hormones. One of these hormone analogs appears to hold considerable promise in prostate cancer treatment and the Cooperative Studies Program is about to initiate a large-scale clinical trial of the effectiveness of this compound. This clinical application of a basic scientific discovery provides an elegant example of how the VA's Research Program can contribute to the entire spectrum of biomedical inquiry.

The Career Development Program in the VA trains young physicians for careers in biomedical research. This is a highly competitive program that supports the training of approximately 200 young physicians who work under the supervision of established VA scientists. As with all research support, applications are evaluated by a panel of national experts in science and research training. The graduates of the Career Development Program become the next generation of leaders in clinical research in the VA. This program is our investment in the future to ensure the availability of a pool of well-trained clinician researchers to head the clinical departments of VA medical centers and to advance the practice of medicine through their research.

Under the "high priority program" category, the VA has on occasion set aside funds for research in selected diseases that are prevalent among veteran patients and provide a special research opportunity. Such activities would come under the targeted research area, and we have examples of two centers for the study of the biological basis of schizophrenia, several programs in basic and clinical research in alcoholism, and studies on the basic biology of aging and cancer.

Periodically, we seek recommendations from VA and academic scientists for new areas for targeted research programs. These recommendations are then reviewed by the Medical Research Service Planning Council and new program initiatives are developed. It may be of interest to this task force that in a recent review our Planning Council recommended targeting scarce research dollars, not for special research areas, but for additional training in basic science for VA clinical researchers. This recommendation reflects a growing consensus in the biomedical research community that future clinical research must be linked more and more with basic scientific inquiry. Good clinical research is now, and will continue to be, the application of the latest basic scientific knowledge and techniques to clinical problems. The VA is seeking a mechanism to allow its clinical researchers to keep abreast of an exploding knowledge base in molecular biology.

I want to say just a word about the research administration in the VA. Some of the features of our program provide strength and flexibility by virtue of the fact that we can accept funds from a variety of sources. While the Medical Research Service in VA Central Office is responsible for national peer review and overall program administration, an Associate Chief of Staff for Research and Development manages the program at each of our large research hospitals. The local Research Offices at VA medical centers are responsible for establishing and monitoring appropriate committees to review all studies that involve human and animal research subjects. I am proud to say that in these areas the VA has been in the forefront in establishing mechanisms to protect the rights of research subjects.

The Research Offices at local VA medical centers administer funds from a variety of sources that support VA investigators. Other Federal agencies—for example, NIH, NIMH, EPA, and DOD—support VA research through interagency agreements, and private institutions such as foundations and industry contribute significant amounts of resources in support of VA scientists. Our flexibility to accept funds from multiple sources results in productive collaborations among Federal agencies and between the Federal Government and the private sector.

I would like to spend the last few minutes by speculating on the future of biomedical research in the VA. I believe the critical challenge in these times of constrained budget is to maintain the opportunity for young physicians to enter careers and research. It will continue to be an unusual physician who embarks on a research career. Training and education will be elongated as the basic scientific knowledge required to do first quality clinical research expands. To attract young physicians into science, there must be not only training opportunities, but a commitment to ongoing, uninterrupted support of the productive investigators. Competition for limited research funds is a useful instrument to assure support of high-quality research. But if competition is allowed to become so intense that excellent, productive investigators cannot maintain their research support, we will not only lose today's researchers, but we will dissuade young people from entering research careers. If medicine is to continue to advance as a science we must be able to attract the best and the brightest medical students to careers in research.

I just wish to thank the Science Policy Task Force for the opportunity to discuss the VA's Research Program.

[The prepared statement of Dr. Greene follows:]

STATEMENT OF
RICHARD GREENE, M. D., Ph.D.
Director, Medical Research Service
Department of Medicine and Surgery
Veterans Administration
before
The Science Policy Task Force of
The Committee on Science and Technology
House of Representatives
April 23, 1986

Mr. Chairman, members of the Science Policy Task Force and ladies and gentlemen. My name is Richard Greene. I direct the biomedical research program of the Veterans Administration. I am very pleased to have this opportunity to describe the VA's medical research effort to this distinguished audience.

The Veterans Administration supports a biomedical research program with an annual budget of approximately $160 million that includes investigation in virtually all areas of biology and medicine. The research is carried out principally by physician-scientists who work in VA medical centers as both researchers and clinicians. VA scientists hold academic appointments at medical schools and universities affiliated with VA medical centers. Funding for individual research studies is based on rigorous peer scientific review by standing committees composed primarily of non-VA academic scientists.

At the outset I should like to mention three aspects of the VA's medical research program that distinguish it from other federal research efforts.

1. The VA's biomedical research program is closely linked to the Agency's patient care mission. To this end we principally support and train physician investigators who pursue research part time while spending the majority of their time caring for patients in VA medical centers. About 75% of the 2500 VA-supported principal investigators are physicians.

2. The VA's research program is intentionally oriented toward clinical investigation. While the VA does support a significant amount of basic biological research, the average investigator in our system is studying the cause and/or the treatment of a disease prevalent among VA patients.

3. The VA's biomedical research program is intramural. We support VA scientists who carryout their studies in VA medical centers. We do not make grants or contracts to private institutions. A major objective of the VA's research effort is to establish a spirit of scientific inquiry in VA medical centers that enhances the quality of patient care.

I would like now to turn to a description of the four programs that make up the VA's medical research portifolio.

A. The Merit Review Program:

The largest portion (75%) of our research funds are expended to support projects conceptualized, planned, and implemented by scientists at VA medical centers. Proposals to undertake such studies are developed at the local level and reviewed by the medical center's R&D Committee and appropriate subcommittees on human and animal subjects. Once approved at the local level the proposal can then be submitted to the Medical Research Service in VA Central Office where it is rigorously peer reviewed in our Merit Review Program. The scientific evaluation of research proposals is carried out by 14 standing Merit Review Committees organized by medical discipline and composed of national experts drawn primarily from academic medical centers. The Merit Review system is organized in this manner to assure that we support only meritorious scientific studies.

The investment of such a large portion of resources in the Merit Review Program reflects our conviction that science and medicine are most likely to advance in a system that 1.) allows scientists themselves to choose the problems that they wish to study and 2.) supports those proposed research projects that peer experts believe are most meritorious. In the VA this philosophy results in the support of 2,000 investigators who work in virtually all areas of biology, medicine, psychiatry and surgery. VA scientists supported by the Merit Review Program are exploring the pathological processes that result in such diseases as diabetes, Alzheimer's disease, schizophrenia, alcoholism and cancer. Other VA laboratories are attempting to develop new and effective therapies for spinal cord injury, heart disease, psychoses, and AIDS, to mention but a few examples.

B. The Cooperative Studies Program:

The Cooperative Studies Program supports large-scale multihospital clinical trials that evaluate promising new medical and surgical therapies. Because the VA's research program is intimately linked to its patient care effort, significant economies are achieved by carrying out controlled clinical trials in the VA medical care system. In evaluating the relative effectiveness of alternative treatments, data must be pooled from large numbers of patients treated with an identical protocol. Such studies can efficiently be performed in the VA medical care system utilizing the expertise in research design and statistical methodology that has been developed in our Cooperative Studies Program.

The VA has carried out some landmark clinical trials that established effective therapies for tuberculosis, psychoses, and hypertension. Examples of current VA Cooperative Studies include evaluation of drugs for the treatment of epilepsy, heart disease and hypertension in the elderly, and the evaluation of new surgical techniques for the treatment of laryngeal cancer and lower limb vascular occlusions.

It is especially rewarding when a basic scientific discovery results in a new therapy that proves effective in a carefully controlled clinical trial. The VA is about to launch a Cooperative Study of the effectiveness in prostate cancer treatment of a new compound developed by one of our outstanding basic scientists, Dr. Andrew V. Schally of the New Orleans VA Medical Center. Dr. Schally's basic research studies on how hormones of the hypothalamus of the brain control endocrine gland function resulted in his receiving the 1977

Nobel Prize in Medicine. Recently Dr. Schally has turned his attention to the development of a series of synthetic chemical compounds that differ slightly from natural brain hormones. One of these hormone analogues appears to hold considerable promise in prostate cancer treatment and the Cooperative Studies Program is about to initiate a large-scale clincial trial of the effectiveness of this compound. This clinical application of a basic scientific discovery provides an elegant example of how the VA's research program can contribute to the entire spectrum of biomedical inquiry.

C. The Career Development Program:

Through the Career Development Program the VA trains young physicians for careers in biomedical research. This highly competitive program supports the research training of approximately 200 young physicians who work under the supervision of established VA scientists. As with all research support, applications are evaluated by a panel of national experts in science and research training. The graduates of the Career Development Program become the next generation of leaders in clinical research in the VA. This program is our investment in the future to insure the availability of a pool of well trained clinician-researchers to head the clinical departments of VA medical centers and to advance the practice of medicine through their research.

D. High Priority Programs:

Under this program category, the VA has on occasion set aside funds for research in selected diseases that are prevelant among veteran patients and provide a special research opportunity. Examples of such targeted research programs include the establishment of two centers for the study of the biological basis of schizophrenia, several programs in basic and clinical research in alcoholism, and studies in the basic biology of aging and cancer.

Periodically, we seek recommendations from VA and academic scientists for new areas for targeted research programs. These recommendations are then reviewed by the Medical Research Service Planning Council and new program initiatives are developed. It may be of interest to this Task Force that in a recent review our Planning Council recommended targeting scarce research dollars, not for special research areas, but for additional training in basic science for VA clinical researchers. This recommendation reflects a growing consensus in the biomedical research community that future clinical research must be linked more and more with basic scientific inquiry. Good clinical research is now, and will continue to be, the application of the latest basic scientific knowledge and techniques to clinical problems. The VA is seeking a mechanism to allow its clinical researchers to keep abreast of an exploding knowledge base in molecular biology.

Research Administration in the VA:

Before speculating on the future of research in the VA, I would like to describe some administrative features of our program that provide its strength and flexibility. While the Medical Research Service in VA Central Office is responsible for national peer review and overall program administration, an Associate Chief of Staff for Research and Development manages the program at each of our large research hospitals. The local research offices at VA medical centers are responsible for establishing and monitoring appropriate committees to review all studies that involve human and animal research subjects. I am proud to say that in these areas the VA has been in the forefront in establishing mechanisms to protect the rights of research subjects.

The research offices at local VA medical centers administer funds from a variety of sources that support VA investigators. Other Federal agencies (e.g. NIH, NIMH, EPA and DOD) support VA research through interagency agreements and private institutions such as foundations and corporations contribute significant amounts of resources in support of VA scientists. Our flexibility to accept funds from multiple sources results in productive collaboration among Federal agencies and between the Federal Government and the private sector.

The Future of Research in the VA:

I would like to spend the last few minutes by speculating on the future of biomedical research in the VA. I believe that the critical challenge in these times of a constrained budget is to maintain the opportunity for young physicians to enter careers in research. It will continue to be an unusual physician who embarks on a research career. Training and education will be elongated as the basic scientific knowledge required to do first quality clinical research expands. To attract young physicians into science there must be not only training opportunities, but a committment to ongoing, uninterrupted support of the productive investigator. Competition for limited research funds is a useful instrument to assure support of high quality research. But if competition is allowed to become so intense that excellent, productive investigators cannot maintain their research support, we will not only lose today's researchers, but we will dissuade young people from entering research careers. If medicine is to continue to advance as a science we must be able to attract the best and the brightest medical students to careers in research.

I wish to thank the Science Policy Task Force for this opportunity to discuss the VA's research program. It is heartening to know that this Task Force is undertaking a comprehensive analysis of the future of our biomedical research enterprise at this critical point in its history.

I would be pleased to answer any questions.

DISCUSSION

Mr. **Walgren**. Would I be right in gathering that the VA Research Program has had a relatively stable level of funding over the last 20 years, if not in increasing funding. Is that correct?

Dr. **Greene**. Well, I think the program began after the Second World War as an effort to get the VA medical centers affiliated with medical schools, and to take advantage of the academic excellence, and I think it has worked very well. The program has been relatively stable in its funding, but there has been very limited growth in the last 3 or 4 years, and obviously this fiscal year has been a difficult year for everyone. It is of interest that, even as we speak, the Supreme Court is hearing arguments on the Gramm-Rudman Act which affected some of us.

Mr. **Walgren**. But would you not be an example of the stability of funding that is asked for by so many other witnesses?

Dr. **Greene**. Well, I think there have been ups and downs which have interrupted the support of some productive laboratories, but I think we have had, in general, stable support. We have been funded in the last 5 years approximately at 2 percent of the patient care budget in the VA, although that has eroded some in the last 2 or 3 years. We are down to 1.7 percent, and obviously to expand or have a moderate expanding program, one needs to have continued inceased support. There has been general stability.

Mr. **Walgren**. Well, would the VA Program be characterized by some of the things that are cited as wished-for attributes in other research areas? For example, a researcher may get a grant in 1 year and not get a grant in the next, and they asked for continued funding or carryover funding or the like. In the VA, with the steady political support that comes with an essentially military-service-related budget, you would not have that problem, and you ought to be able to see the benefit of continuity of your researchers. Is that true?

Dr. **Greene**. Well, I can't compare at the moment the stability of funding, but of course our investigators must go through a peer review process every 3, 4, or 5 years, and people do lose funding based on the competition for funds, so it is not as if once one was in the VA that one is guaranteed continued support. And, as dollars have become tighter relevant to the quality of proposals that are being submitted, there is certainly a reduction in the percentage of applicants who can be supported. So good quality studies are going unfunded, and some laboratories are being interrupted.

Mr. **Walgren**. Has anybody ever done comparative studies of the research results or progress by some measure in the VA versus a similar number of researchers in other similar medical circumstances?

Dr. **Greene**. I know of no such study, but I would just hasten to add that such efforts to evaluate any investment in biomedical research are very complex.

Mr. **Walgren**. In your instance, for example, you have a very high component of what Dr. Marks was asking for, which is the combination physician-principal investigator, and I guess my question would be is there some way of looking at what the history has been where you have a high factor or a high presence of that factor in a way that we could appreciate the benefit of it?

Dr. **Greene**. Well, I know of no formal activity or of an approach that would allow that, but I think that what one could look at is certainly the contribution to the medical literature that comes from our investigators. I think that most people would agree that there is really a disportionately high contribution to the clinical research literature, given the relatively small dollars. Virtually any issue of any clinical journal will have a rather substantial contribution from VA investigators. We have not, obviously, invested as heavily in the basic biological studies so that the whole focus has been on the clinical side.

Mr. **Walgren**. What about any ability to assess the effect of targeting moneys? Now, in a certain sense you are targeting because you are serving a population with some relatively specific needs, for example, the military has a greater interest in spinal chord research than does a wide ranging—I don't know what word to use. But the point is, when you target your moneys, what is the experience in real progress?

Dr. **Greene**. I would agree with the previous speakers that targeting is something that can be done effectively in unusual circumstances, but our basic philosophy is to support the best quality research that is conceptualized by investigators. We do periodically ask experts to identify special opportunities and screen such opportunities for possibly targeting money, and we have kept that level at the 5- to 6-percent of our budget. I think some very useful program have been suggested in this area such as centers to study the biochemical basis of schizophrenia.

It is very, very difficult to judge whether targeting such funds is a better investment than funding 10 more investigator-initiated researchers. I should add, though, that one of the key issues about targeting that we feel strongly about is if one targets in an area such as schizophrenia. The investigators should be the ones that design the studies, and this should be an open competition among investigators who are working in a particular area, as opposed to studies designed, for example, by administrators.

Mr. **Walgren**. Well, thank you very much for your contribution to this and we look forward to being in contact with you as we go along.

[Questions and answers for the record follow:]

SCIENCE POLICY TASK FORCE

Hearings on Policies for Biomedical Research

April 23, 1986

Followup Questions for Dr. Richard J. Greene

1. **You mentioned that the VA used the peer review method for funding deserved intramural research programs. Does this function much like that of the NIH? Are other methods of quality control used either centrally or at the local hospitals?**

The VA procedures for evaluating the scientific merit of research proposals are very similar to those followed by the National Institutes of Health. The key centralized component of this evaluation process is conducted by 14 standing peer review committees (Merit Review Boards) in the following areas: Alcohol and Drug Dependence, Basic Sciences, Mental Health and Behavioral Sciences, Cardiology, Endocrinology, Gastroenterology, Hemotology, Immunology, Infectious Diseases, Nephrology, Neurobiology, Oncology, Respiratory Disease, and Surgery.

Because the VA Merit Review Boards must evaluate projects in relatively broad areas of biomedical research, they rely heavily on additional written ad hoc reviews of proposals. Each proposal is evaluated by two ad hoc reviewers with expertise specific to the proposal being reviewed. Their written reviews are submitted to the Merit Review Board members and also read aloud at the time of the Borad meeting. It should be noted that the great majority of the Merit Review Board members are academic scientists who are not VA employees.

In addition to the centralized review process described above, each proposal must be reviewed for scientific merit and approved by the VA medical center submitting the proposal prior to submission to VA Central Office. Moreover, those proposals involving human participants or animal subjects must also be reviewed by the local medical center human subjects or animal subjects subcommittee of the Research and Development Committee.

2. **You described the involvement of VA hospitals in many different types of clinical trials. What proportion of funds are used for this purpose? Has the VA entered into more collaborative clinical trials with other medical centers, given the increasing costs of such studies and relatively stable patient population at the VA? How reliable is such data from these trials, given that the VA patient population does not reflect the population as a whole?**

The Cooperative Studies Program, which supports multi-hospital clinical trials, utilizes 8 percent of the Medical Research Service budget or approximately 12.5 million dollars. It should be noted that the Cooperative Studies Program is only one of several mechanisms by which clinical studies evaluating new therapies are carried out in the VA. VA clinicians/scientists participate in clinical trials supported by other Federal agencies and by industry. Thus, for example, the Center for Disease Control has recently funded a clinical trial to be conducted in the VA evaluating

Rimantadine, a promising antiviral agent designed to treat influenza in chronically ill elderly patients. The Department of Defense is about to fund a large scale trial in the VA of two antiviral agents for the treatment of AIDS and, finally, the VA medical centers at San Antonio, Texas and Hines, Illinois were chosen to be part of a six center group to evaluate interleukin II, an experimental treatment for cancer. These examples illustrate how the VA participates in clinical trials in which non-VA treatment centers are also involved. Many similar examples could be given of industry supported drug evaluations.

Although the generalizability of the results from clinical trials conducted in the VA is undoubtedly limited by the characteristics of the VA patient population, we do not regard these limitations as serious. The VA population is indeed enriched with patients with chronic disease; however, the clinical trial results are always interpreted with the unique features of the VA population taken into account. On the positive side, the VA population is particularly suitable for evaluating experimental treatments for chronic disease in male patients.

3. **How many physicians compete for positions in the Career Development Program? Do they represent a cross-section of deserving individuals from quality institutions? How many of these physicians-in-training remain at the VA? Is there a mechanism for assuring that the VA does not become "inbred" with respect to the researcher population?**

Each year around 250 physicians compete for positions in the Career Development Program. While applications are welcome from all VA medical centers, most of the applications originate from the 50 to 60 VA medical centers that are most closely affiliated with medical schools. The applicants reflect a nationwide cross section of physicians, representing surgery, psychiatry and the subspecialities of internal medicine. Sixty to 70 percent of the physicians in the Career Development Program remain in the VA 1 year or more after their Career Development appointment ends. Except for the eight Senior Medical Investigators, Career Development appointments are time limited, nonrenewable and nonextendable. This assures a continual influx of new applicants into the different levels of the program. Finally, it should be noted that the members of the Committee evaluating Career Development applications, like the members of the Merit Review Boards, are predominantly academic researchers who are not VA employees.

Mr. **Walgren**. Let's turn, then, to Dr. Frazier, who is the present Director of the National Institute of Mental Health. Dr Frazier, with apologies for the lateness of the hour and appreciation for your having been so patient, please go ahead and verbally focus for the record on points that you feel really ought to be made, and we would love to hear you.

[A biographical sketch of Dr. Frazier follows:]

Shevert H. Frazier, M.D.

Director, National Institution of Mental Health, Alcohol, Drug Abuse, and Mental Health Administation, U.S. Department of Health and Human Services.

Shevert H. Frazier, M.D., assumed the directorship of the National Institute of Mental Health (NIMH) on December 4, 1984. NIMH, a component of the Department of Health and Human Services' Alcohol, Drug Abuse, and Mental Health Administration, is the world's largest mental health research support program, with an estimated 1985 operating budget of $283 million.

Dr. Frazier came to NIHM from Harvard Medical School, where he was Professor of Psychiatry and Psychiatrist in Chief at the school's affiliate McLean Hospital in Belmont, Massachusetts. His career previously encompassed a rich array of experiences in clinical practice, academic and public administration, and professional affairs.

A native of Louisiana, Dr. Frazier received his undergraduate and medical degrees from the University of Illinois. After serving as a medical officer with the U.S. Navy from 1944 to 1946, he established a private practice of medicine in southern Illinois. In 1951, he moved to the renowned Mayo Clinic in Rochester, Minnesota, where he accepted a fellowship in internal medicine and, subsequently, psychiatry. He moved to New York for the first time, in 1958. There, he engaged in research at the New York State Psychiatric Institute, in clinical duties at the Presbyterian Hospital of New York, and in teaching at Columbia University, College of Physicians and Surgeons.

Only four years later, Dr. Frazier was recruited to direct what is now the Texas Research Institute of Mental Sciences in Houston. Over the next few years he served also as Psychiatrist in Chief at Ben Taub General Hospital in Houston, Professor and Chairman of the Department of Psychiatry at Baylor University, consultant psychiatrist to the Veterans Administration Hospital in Houston, and Commissioner of Mental Health and Mental Retardation for the State of Texas.

Dr. Frazier returned to New York in 1968; there, he served as Deputy Director fo the New York State Psychiatric Institute and assumed a variety of senior faculty positions in the Department of Psychiatry, Columbia University. In 1972, he moved to Boston where he remained twelve years in the positions noted previously.

Experienced in psychiatric and neuobiologic research, certified in psychananalysis, and trained in the diverse administrative spheres of academic, hospital management, and state government, Dr. Frazier brings an impressive array of skills to the direction of the national mental health program. At a time when the Federal program is emphasizing the conduct and support of research and rechannelling its former direct involvement in service delivery and professional training into an emergent national leadership role, his broad perspective on issues confronting the mental health field will be invaluable.

STATEMENT OF DR. SHERVERT H. FRAZIER, DIRECTOR, NATIONAL INSTITUTE OF MENTAL HEALTH, ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ROCKVILLE, MD

Dr. **Frazier**. Thank you, Mr. Chairman. I appreciate the opportunity to be here today to testify. I will keep my oral remarks brief and request that my prepared statement be entered into the record.

Mr. **Walgren**. And that is without doubt exactly what is going to happen with all the written submissions, so feel free to focus on individual thoughts.

Dr. **Frazier**. I would like to begin by saying that less than $3 billion has been spent on mental health and addictive research since

1948 by the Federal Government. This is a relatively small amount of money for which I think the Federal Government and the research establishment have made a remarkable return on investment. The National Institute of Mental Health was established following World War II because of the excessive number of neurospsychiatric cases identified in the Selective Service process. It is pretty clear that we have made some progress, but not enough. We have spent less than $3 billion yet we have a group of illnesses which affect 1 out of 5 people. This includes substance abuse, alcoholism, and mental illness. This number is based on research and surveys conducted through the epidemiological catchment area studies which were reported in November 1984.

In the period of time since 1948, we have developed a diagnostic system. We have come from the Dark Ages in mental illness to the present. We have developed a clinical epidemiological program with predictable methods of making diagnoses. We have developed treatments for depression, treatment for psychosis, treatments for mania, and management regimes for a number of illnesses for which we do not have treatments. In addition, we have developed new knowledge on how the brain operates and how the brain, in its operation, effectively changes and alters human behavior—this is especially true in the area of opiate receptors. I think these gains are important.

The NIMH approaches mental health and mental illness from other perspectives. Like other categorical Institutes, our interest is also directed at knowing how the various systems of the body talk to one another, and that includes how the central nervous system and the endocrine systems and immune systems communicate and how these interactions influence behavior. This focus, I think, gives us some special ways of looking at things and also sets different kinds of research priorities and policies.

I want to talk about some issues that your committee has stated an interest in: how we establish research priorities. It is very clear that we have a complex method, but we use the research scientists in the field as the principal knowledge source. We listen also to congressional intent, what Congress feels the people want and, what we understand the needs of the people are. We also have a National Mental Health Advisory Council. Each of the Institutes has an advisory council, and these councils are composed of scientists and nonscientists, who offer their opinions and attitudes and input.

We also pay attention to the advice of other established bodies, such as the extramural and intramural research review boards. We also pay attention to the President's budget.

The early emphasis in NIMH was on services, and though it was a part of NIH up until 1967, it really had a major services orientation. The research presence was there but not very well focused. It is only in the last two decades that the research enterprise has been focused more sharply. In the last decade that focus has become oriented very much toward the rigorous scientific designs of the neurosciences and the behavioral sciences. This has resulted in our basic research divisions concentration on the interaction of health and behavior and how behavior alters health, since about 50 percent of mortalities are based on some alterations in lifestyle which contribute to death.

In establishing priorities, we pay attention to the needs of people. I couldn't help but think of children and youth when Howard Hiatt was talking about how we have not paid enough attention to the needs of the mentally ill. This is especially unfortunate with regard to substance abuse because it essentially is a disease of youth, a disease of adolescence, as is depression. Depression is a growing concern with regard to childhood and adolescence. We see it in young adults, and we have suicide, among the youth today which is a very big issue.

As we establish these priorities, we are attentive to the needs of the people but it is very clear that only scientists who are actually conducting research can establish where science needs to go and where it will go. I think we need to pay attention to that. I think that the direction of science is determined by the interactive communications among and between various diverse scientists who come together on a regular basis and discuss the nature of the problems and the nature of the state of the science, the timing of interventions, and how we ought to build programs. The Institute also tries to have people look at the entire scope of the field and find out where gaps exist, and how we ought to seed those areas and provide some program development, to make those areas come alive, and when the time comes, to begin to cross-fertilize ideas and contributions in those particular areas.

We don't know where the new knowledge is going to arise from. It may be from basic or clinical studies. For that reason, I would hope that we wouldn't foreclose on any particular area of research on brain function, or behavioral function, or the interactive attitudes of human beings with the environment, because all of these are a part and parcel of how mental illnesses and mental disorders occur.

In the process of selecting research projects to support, the Institutes tries to keep a focus on where the research is and where findings are occuring. It is clear that scientists are like other human beings. When they have the beginnings of an awarenesses, the ripening of ideas, or the beginnings of creative interventions, they tend to focus and come together in those areas. It becomes easier to recruit people in an area of science where there is a rapid expansion of new knowledge. We pay attention to that in selecting projects for support.

It is pretty clear that while there have been a lot of Nobel laureates and Lasker awardees, the NIMH has been fortunate to have three Nobel laureates and four Lasker awardees, and for a relatively young group of sciences, I think that is an important achievement.

We have identified some problems in the mechanisms by which we review and rank applications, but they are not severe. We have inflation in the assigning of scores. We have also had some problems in the nature of comparing quality of output, and quality of science. We are looking at other methods of reviewing applications through in the peer review system. I think the review process is good but we will improve it.

We have need for more flexibility in funding mechanisms to attend to the needs of the scientists by providing mechanisms which will make it easy for the scientist to develop what they need to evolve. I think the tyranny of the RO-1 enterprise has probably peaked out, and maybe the time is coming for trusting the direction of science with an overview, a trusteeship, a kind of review process that watches carefully about how the stewardship of the money is being carried out.

In supporting the activities of research scientists, I would like to point out that we need to lengthen the term of support of research. The fact that the average ADAMHA grant receives 3 years of support, or less is counter productive and not economical in that a scientist must spend about a third of their time preparing the next grant application. I think this is essentially thwarting some investigative activity. I believe it would be important to provide the flexibility to increase the length of funding to the 5- to 7-year range.

The other problem we have is getting information out from the laboratories to the practitioners. This is an important issue for ADAMHA because we have vast constituencies of individuals who are interested, and passionate, and fervent, about what research we are doing, and how we ought to be doing it.

A good example of where we have not been entirely successful is lithium carbonate. It was discovered as a treatment for mania in 1949. It was not until 20 years later—and that's about 15 years ago—that the treatment was out in the field where people could use it. The communication process, though it is improving, has not improved enough so that clinical applications of new research activities and findings reach the broad mental health field efficiently.

I would like to turn to the future of biomedical research. Obviously research is dependent on scientists and the brain power you have and the ability to attract and recruit young scientific personnel. This is the name of the game. It takes 8 to 10 years to develop mature research scientists, autonomous and independent, and in order to do that, we have to start filling the pipeline with the brightest and the best talented young physicians, young scientists, young Ph.D.'s now.

It is shortsighted to cut down on research training in my view. The future of biobehavioral neuroscience activities is going to be dependent on recruiting the best brains, introducing them to the field, supporting them, and giving them stability and predictability with regard to resources. That means when the funding cycle changes, fluctuating up and down, that there still will be a mechanism that allows for stability and maintaining the presence of a laboratory. You can't just collect a bunch of scientists together and then have the funds play out. Then what do you do with them? They have to work and live and eat, and they also need a place to have a predictable future, and I think we need to pay attention to that in science policy.

The other thing I think we pay too little attention to is the climate of freedom to think and pursue new ideas. That's exactly what science is all about. You have got to have that extraordinary ability of an institute, or a research enterprise, or a hospital, or a laboratory, or a medical school, or a university, to provide an academic environment that allows the freedom to think, the freedom to pursue ideas, the freedom to get fired-up to communicate, to cross-communicate, to fertilize. This is an invaluable resource. It is clear it is expensive, but we need to pay attention to that climate. Thank you.

[The prepared statement of Dr. Frazier follows:]

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Statement of

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National Institute of Mental Health

before the

Science Policy Task Force

Committee on Science and Technology

U. S. House of Representatives

April 23, 1986

Mr. Chairman and members of the Committee, I am Shervert H. Frazier, Director of the National Institute of Mental Health. I am pleased to have this opportunity to talk with you this morning about policies for biomedical research. The National Institute of Mental Health is one of the oldest programs within the Federal biomedical research establishment--only the National Cancer Institute is older. Authorizing legislation for NIMH, Public Law 79-487, was passed in July, 1946. We are planning to celebrate our fortieth anniversary by holding a two-day scientific symposium in June, at the National Academy of Sciences.

Our sister Institutes in the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) - the National Institute on Alcoholism and Alcohol Abuse and the National Institute on Drug Abuse - are also long-term supporters of biomedical research. These two Institutes were established in 1970 and 1972 respectively. However, the federal support of biomedical research on alcohol and drug abuse had its beginnings within NIMH in 1946. Although our biomedical research programs differ to some degree, all three Institutes have a common and major interest in the central nervous system. Much of what I say here this morning applies to all three Institutes.

My review of the questions you asked to be addressed in these hearings leads me to focus my remarks on five major concerns: (1) establishing research directions and priorities; (2) selecting projects for support; (3) employing appropriate funding mechanisms; (4) applying research results to clinical problems; and (5) charting the future of biomedical research.

RESEARCH DIRECTIONS AND PRIORITIES

The process of establishing research directions is as much an art as it is a science and it is as political as it is scientific. As with all decisions, the determination of research directions is made under varying conditions of uncertainty. At a general level it involves judgments about the reliability and validity of existing knowledge, the magnitude and tractability of the unknown, the methods to be used in the pursuit of knowledge, the availability of economic, technological and personnel resources, the perception of the clinical problem, the incidence and costs (both in human suffering and economic terms) of various diseases, and the pressure exerted by scientific, political and client groups. The sources of information consulted are many; the amount of information provided is extensive.

Long-range planning for research priorities in the Institute involves formal and informal input. In the NIMH we have established an Office of Policy Analysis and Coordination specifically charged with developing policy positions, overseeing program evaluation efforts and coordinating planning efforts within the Institute. As a part of its functions, this office seeks advice from a number of sources with varied backgrounds. Primary among these are senior, highly respected, non-government scientists whom we seek out in our periodic review of research programs within the Institute and ask to provide advice on the research directions and scientific initiatives of our programs. The other ADAMHA Institutes have similar mechanisms for obtaining science advice. More in-depth analyses of specific areas within our programs are usually managed by program staff and similarly involve primarily non-government scientists, many of whom are not supported by the Institute, to critically and objectively review issues of programmatic interest.

Research supported by our extramural programs is also strongly influenced by scientists in the field. Our research programs seek to involve research scientists in priority setting through their participation in planning meetings, workshops and conferences; writing state-of-the-science papers; serving on evaluation teams; submitting research applications; conducting research; and reviewing applications submitted by others. Scientists in the field also play substantial roles in what has become known as Institute-directed research by identifying special needs that they feel are not met by the regular grant support mechanisms.

In our intramural research program, research directions emerge from the results of some 270 projects conducted each year in 19 laboratories by some 400 staff scientists, research fellows, associates, and visiting scientists from this country and abroad. Close collaboration with researchers in the National Institutes of Health provides another source of direction. In addition, each intramural laboratory is reviewed every three years by a Board of Scientific Advisors composed of scientists from the field.

Three other major sources of influence on all NIMH research programs are the President's Budget, Congress, and the National Advisory Mental Health Council. The President's Budget establishes the overall parameters for the budget request in the context of available resources and national priorities. As you well know, Congress determines the appropriated level of support, and mandates programs in response to the needs of the public. In recent years, Congress has expressed interest and support for specific types of research, has sought to establish the number of new regular grant awards, and used priority scores as a means of comparing the scientific excellence of different programs. The National Advisory Mental Health Council, whose members include both scientists and non-scientists, reviews the overall policies and programs of the Institute, and serves as the second step of our peer review for grant applications.

The major strategy guiding NIMH research programs for a number of years was — fund as broad a range of research as possible. Since it is hazardous to predict where breakthroughs will occur, maintaining a broad research portfolio made a great deal of sense. More specific needs were addressed through research initiatives that produced the Epidemiological Catchment Area Program, the Clinical Research Centers, and the Research Scientist Development Awards. Nevertheless, the emphasis on support for a broad range of research fostered the perception that the mental health portfolio had become too diffuse and that NIMH was placing inappropriate emphasis on some topics that were only tenuously related to mental illness and mental health. It was evident that the field had to be narrowed and new priorities had to be established.

The foundation for the priorities was found in the evaluation activities of the NIMH, a 1984 Institute of Medicine (IOM) report commissioned by ADAMHA, and a PHS initiative on health and behavior, as well as ongoing liaison of Institute staff with constituency groups, professional organizations, and concerned citizens. The evaluation activities undertaken by our own Neurosciences Branch and Behavioral Sciences Branch resulted in reports that emphasized the importance of these sciences for mental illness and identified promising research areas and methodologies. The IOM report, "Research on Mental Illness and Addictive Disorders: Progress and Prospects", acknowledged the progress made in schizophrenia research, but also detailed its limitations. In addition, it cited the overwhelming needs related to mental disorders of childhood and adolescence and pointed out that much of the existing information about brain function, behavior, and mental disorders may not apply to the elderly, a rapidly growing segment of our population. The PHS initiative concerned the relationship between health and behavior. Government statisticians have estimated that 50 percent of the mortality from the ten leading causes of death in the United States is attributable to aspects of life style. In addition, the IOM report indicated that behavioral factors are crucial in the development of and management of chronic diseases -- the main contributors to the burden of illness in the United States and other industrialized nations.

In developing the Fiscal Year 1987 research plan, NIMH identified five priority areas: schizophrenia, mental disorders of childhood and adolescence, mental disorders of aging, the link between health and behavior, and basic research in the neurosciences and behavioral sciences. This plan is reflected in the 1987 budget where the redistribution of support into these priority areas begins. In addition, the recently completed reorganization of the Institute reflects these priorities: the new Division of Basic Sciences contains branches for the neurosciences, the behavioral sciences, and health and behavior; the new Division of Clinical Research includes branches for schizophrenia, mental disorders of childhood and adolescence, and mental disorders of aging.

Changing from an internal structure based more on discipline to one focused on disorder, it is now possible to address Institute priorities more directly in three ways. First, our new structure clarifies the mission and research directions of the Institute. Second, the new structure will enhance significantly our ability to shepherd our resources carefully, to build new initiatives on existing ones. Third, our attempts to reorganize, to slim down, to chart a course, may encourage some of the major research laboratories and centers of research to do the same.

SELECTING PROJECTS

The selection of projects for extramural support is based on priority scores assigned by peer review, established Institute priorities, and program balance. The NIMH maintains an array of initial review groups (IRGs) composed of researchers in the field. These groups meet at least three times a year to evaluate the scientific quality of submitted applications. The applications are sent to IRG members prior to each meeting. During the meeting, IRG members make two decisions regarding each application. The first is to recommend approval or disapproval of an application; and the second is to determine the priority score, an assessment of the absolute quality of the research, which is assigned to each application approved.

Following the second review for overall policy issues by the National Advisory Mental Health Council, applications recommended for approval and their priority scores are forwarded to program staff for possible funding. Funding decisions involve research priorities and program balance as well as priority scores. NIMH requires 90% of all awards within a Branch to be based on IRG and Council priority score order. The remaining 10% may be funded out of priority order, but in each case funding of each project must be specifically justified by program staff and reviewed at the Division and Institute levels.

In our intramural program, project selection is based on proposals submitted by staff scientists that are reviewed by section and laboratory chiefs, and the division director. In addition, each laboratory and each scientist undergoes periodic review by a Board of Scientific Counselors composed of senior scientists in the field.

Generally, these systems for assessing scientific merit have served us very well. Three Nobel laureates and four Lasker awardees are among our grantees and intramural researchers(1). A somewhat dated but unique analysis of the life sciences literature between 1965-78 found NIMH grantees and intramural scientists well-represented among the most-cited investigators in the fields of cell biology, pharmacology, neuropharmacology, and psychiatry.

Some problems, however, are developing in our extramural review system. Senior investigators are becoming increasingly reluctant to serve on IRGs. Service on an IRG entails a four-year commitment, a heavy work load, and inadequate compensation for the work performed. Another concern is that "inflation" is occurring in priority scores. While there is reason to believe that some of this is due to increased quality of applications we receive (-- a function of increased pressure on investigators to produce better applications and the weeding out of less competitive investigators), part of this is undoubtedly due to the reduction in the number of awards made and the need for increasingly better priority scores for funding. In addition, the range of scores used by IRGs is narrowing. This concentration of applications into a smaller and smaller range of scores is making it increasingly more difficult to discriminate between approved projects on the basis of priority scores alone. We are currently examining, at both the Institute and Agency levels, the structure and functioning of our review system because its effective operation is critical to the mission of the Institute.

FUNDING MECHANISMS

Each ADAMHA Institute employs a wide range of funding mechanisms for support of research and research career development: regular project grants, small grants, centers, research scientist development awards, cooperative agreements, contracts and inter-agency agreements. These mechanisms, in aggregate, are designed to facilitate the conduct of research under the varying conditions posed by such a complex undertaking as biomedical and behavioral research.

These mechanisms address different aspects of the research endeavor. Regular project grants which constitute about 80% of our extramural program, support discrete, limited studies performed by one or more investigators, usually from the same discipline and generally in a single setting. Small grants which last only one year are designed to provide funding to young investigators and give them an opportunity to perform pilot work preparatory to submission of a regular project grant.

Research centers provide support for multidisciplinary teams of researchers working in related research areas. Frequently, such support includes funds for core facilities and services, common scientific or diagnostic instrumentation, and sophisticated data management and data analytic support. Centers also provide excellent opportunities for research training. Center grants thus provide a foundation for a wide ranging and coordinated research effort. However, the viability of research centers depends upon the ability of their research teams to successfully compete for regular project grants.

Research Scientist Development Awards are career support mechanisms geared to provide long term salary support to researchers at various stages of their careers. These funds are meant to free investigators from the burdens of clinical, teaching, or administrative responsibilities so that they can devote near full time to research pursuits. Career mechanisms available include the Research Scientist Development Award, Research Scientist Award, Clinical Investigator Award, and the Physician Scientist Award.

In addition to the career development awards already mentioned, NIMH tries to encourage and support the development of new generations of researchers through pre- and post-doctoral fellowships, and institutional training grants. Special attempts are made to attract minority individuals to research careers through the Minority Access to Research Careers Program, the Minority Biomedical Research Service Program, the Minority Fellowship Program, and the Historic Black College Program.

Cooperative agreements are joint ventures between researchers in the field and Institute staff to develop research in high priority areas that cannot be developed by the field alone. This research is usually targeted, conducted at more than one site, and its methodology standardized through the use of a common protocol.

Research contracts are Institute initiated support of specified research and research support activities. Research support under this mechanism is targeted to a specific research need or research support activity with specified products to be delivered. Inter-agency agreements permit agencies to jointly support a project or allows one agency to add its requirements to a project already underway in another agency, thereby, eliminating the need to support a separate project.

The choice of a funding mechanism most likely depends on the nature of the task, the conditions under which the task is to be performed, and the organized effort it requires. A given area of research will require a different mix of funding mechanisms at different stages in the development of knowledge and methods, and under different conditions such as the availability of manpower and other resources, public health urgency, and the nature of the research itself. Some funding mechanisms may appear more appropriate than others because they are more frequently used or because the productivity of the research they support is more visible.

Although the bulk of our extramural support of research is in the form of regular project grants, it is clear that 1) the research enterprise requires a variety of mechanisms to meet different needs, and 2) that needs change over time with developments in science and in public health. New funding mechanisms may need to be considered for such purposes as the replacement of obsolete equipment and facilities, the retraining of experienced investigators in new technologies, supporting the conduct of longitudinal research, ensuring the availability of research materials, and responding to emergency situations. A review of funding mechanisms is currently underway at the Agency level.

Our intramural research program offers an environment that has some unique characteristics. It provides the opportunity for collaborative research, supports a critical mass of investigators, provides support for research that is hard to conduct under extramural auspices (e.g., longitudinal research, high risk research, research that can take advantage of rapidly developing technologies, and research that rapidly responds to emergency situations). The intramural environment also provides an excellent resource for research training.

While the need for flexibility in the use of different types of funding mechanisms is important, an effective support system also requires some measure of stability and attention to efficiency. Existing mechanisms provide support for one to five years. At least in part because of the conservatism of review committee members in response to more limited funds, the average duration of support for regular grants is about three years. This means that investigators are required to devote a considerable amount of their time to applying for support. It also means they are always faced with the problem of dividing their research into "fundable units" rather than concentrating on the development of what may be more productive strategies of research.

APPLYING RESEARCH RESULTS

The link between research and clinical practice has been a critical part of the developments in mental health care at least since 1946 when NIMH was established. In the immediate post-war years, the successful experiences of the military in providing rapid, front-line treatment to psychological casualties stimulated research to develop and refine forms of brief psychotherapy. The payoff from this line of research over the years has been considerable.

When the new psychoactive drugs came in, their value in research as well as in therapy was recognized and seized upon immediately and in a multitude of ways. The need to determine safety and efficacy prompted the development of a sophisticated methodology for controlled clinical trials. This methodology has been applied in all areas of medical research and is being used now in studies of the effectiveness of psychotherapy.

Drugs also have proved useful in validating diagnoses and in subtyping diagnostic categories. Progress in this area has been associated with advances in describing and classifying mental disorders.

One measure of progress is seen in the evolution of the mental health care system. Thirty-five years ago, the care picture was bleak. Nearly 80 percent of mentally ill patients were consigned to large public institutions for extended periods of time. The hospitals were understaffed, treatment capacity was minimal, the quality of care was often dismal.

Contrast that with the current state of our mental health service delivery system. While the number of episodes of care has increased more than ten-fold, the ratio of outpatient to inpatient care has been reversed. We see a system comprised of numerous elements--an increasing mix of public and private sources of care; increased interaction between specialized mental health and general health care resources; and a variety of outpatient settings providing mental health services. There is now an impressive array of effective treatments for many of the most severe mental disorders.

About 80 percent of depressive patients can now be treated effectively by antidepressants, monoamine oxidase inhibitors, electroconvulsive therapy, psychotherapy or a mix of these treatments. For some types of depression, novel therapies, such as full spectrum light treatment, are also being investigated. Neuroleptics are effective in treating such symptoms of schizophrenia as hallucinations and delusions. Psychotherapy and antidepressants are useful in the treatment of phobias. It is estimated that the use of lithium in the treatment of manic-depressive illness has saved more than $6.5 billion in the last fifteen years. In contrast to this savings related to a single disease, it is interesting to note that the United States has spent less than $3 billion on all mental health research since 1948.

It would be impossible to cite all contributions of research to patterns of clinical care and the refinement of treatment. I simply want to point out that directions taken in mental health care over the past three to four decades have been informed by research. We have a more precise diagnostic system, a broader and more effective range of treatments that increasingly can be tailored to individual clinical needs, and an improved ability to identify service needs.

This record reinforces my strong conviction that basic research is absolutely essential to advances in clinical research and treatment and to progress in prevention. I see no other choice but to base a biomedical research program on basic research. Let me illustrate. The work on brain receptors has demonstrated the over-simplistic nature of many theories regarding the mechanisms of action of psychotropic medications. But in doing so, it has suggested what needs to be done to make drugs more potent while reducing their side-effects. We now have the capability to develop new drugs in the laboratory, by finding substances that selectively bind to the relevant receptors or are sufficiently similar at the molecular level to the target receptors to affect their function. This process of engineering drugs radically reverses the traditional process of drug development where drugs are discovered clinically and then studied in order to determine how they work.

I do not wish to imply that the relationship between basic research, clinical research and treatment, and prevention is one-way. We believe that basic research holds the key to the ultimate prevention and cure of mental disorders, but that clinical research directed to the alleviation of the immediate suffering of the mentally ill and those whose lives they affect, is an equally important part of our mission. The relation between basic and applied research is seen as reciprocal, the knowledge generated by one feeding the conceptualization and implementation of research in the other. Of course, it is always necessary to use caution when moving from the findings of basic research to clinical application, but wherever possible we encourage the formal integration of both kinds of research in the same project, as in our Clinical Research Centers program and in our Intramural research program.

FUTURE OF BIOMEDICAL RESEARCH

What can be said about the future of biomedical research depends on the time frame one has in mind. If it is the next year, it's exciting; the next decade, it's inspiring.

I have touched on the importance of biomedical research and some general problems which it involves. I would like to center these remarks on the future of brain research -- a subfield of biomedical research that is central to the mission of the three ADAMHA Institutes. Despite all we know about the brain, our knowledge remains elementary. The future of brain research depends on the priority it is given. The return on such an investment could be staggering. In 1971, the direct and indirect expense of schizophrenia alone was estimated to be $19.5 billion. The estimated cost for all cancers was about the same. In 1971 research on the brain and mental illness was just starting to come together. Now, with the virtual explosion of new techniques and conceptualizations of brain function, the potential can be realized. The estimated cost to society in 1983 of mental illness was $70 billion--$33 billion for treatment and support and another $37 billion for related costs. Research on brain and mental illness now merits a level of support that is comparable to the support given to other body systems and physical illnesses.

As investigators delve more deeply into the intracellular mechanisms and the genetic regulation of neural processes underlying behavior, research requires a higher level and number of skills as well as more advanced technology. Research is becoming more expensive. We are already supporting research employing sophisticated brain imaging technologies such as Positron Emission Tomography (PET) and Nuclear Magnetic Resonance Imaging. In developing the technology that made the PET scan possible, Dr. Louis Sokoloff, NIMH staff scientist, drew on such disparate fields as mathematical modeling, physics, enzyme kinetics, and computer imaging.

This illustrates the complexity of understanding how the brain controls behavior. Comprised of 10 to 100 billion cells, the brain is the most complex organ in nature. At any moment, each cell, or neuron, is receiving, simultaneously, as many as a thousand impulses from adjoining cells and transmitting thousands more. Trillions of connections are involved. It is estimated that 300 or more neurotransmitters exist in the brain. We have identified about 60 to date. The role of the endocrine and immune systems in brain function is even less understood. The challenge of the future is to increase our understanding of the organization and functioning of these numerous and diverse elements and systems so that we can unravel the mysteries of the human mind and more effectively treat and prevent mental illness.

Given the magnitude of the task, the uncertainty of the path, and the potential for payoff, the guiding principles for policies related to brain and biomedical research should be - flexibility, facilitation, and clarity of goals.

ENDNOTE

1. Nobel Laureates cited in text as supported by the NIMH are:

    Julius Axelrod - 1970
    (Nobel Prize in Physiology & Medicine)

    Herbert A. Simon - 1978
    (Nobel Prize in Economics)

    Roger W. Sperry - 1981
    (Nobel Prize in Physiology & Medicine

    Lasker Awardees cited in text as supported by the NIMH are:

    Solomon Snyder - 1979
    (Lasker Award in Basic Research)

    Jerome Frank - 1981
    (Lasker Award in Clinical Research)

    Louis Sokoloff - 1981
    (Lasker Award in Clinical Research)

    Eric Kandel - 1983
    (Lasker Award in Medical Research)

DISCUSSION

Mr. **Walgren**. Thank you very much, Dr. Frazier.

As I understand it, cancer draws $300 a year research per patient, schizophrenia, $7 a year.

Dr. **Frazier**. $7 a year.

Mr. **Walgren**. Why is that?

Dr. **Frazier**. Well, mental health diseases are stigmatized diseases. You have to pay attention to what people feel about them. It is only in the last 5 years that mentally ill patients and their families have come "out of the closet." They are able to talk about their illnesses now. The growth of the National Alliance of the Mentally Ill is phenomenal; a new chapter every 36 hours. It is very clear that people are up to talking about the fact that they have mental illness in their families, and they are not afraid of disclosing it anymore. Cancer was the same way 20 years ago. People didn't talk about having cancer, and TB before that. The stigma moves along from decade to decade, and it comes and goes in cycles also.

Mr. **Walgren**. How do you decide how much to put into one interesting idea, as opposed to another interesting idea. I gather in the area of mental health, you have a whole host of different cancers, probably a less common foundation in mental health than in what I guess we would hope to find as common fundamental causes in cancer, so you are put to this problem of allocating your resources, and I gather there are interesting ideas in all the areas. How do you decide how to make that distribution?

Dr. **Frazier**. It is done with the advice of the leading scientists in the world in a specific research area, plus the other scientist in affiliated fields. Other Institutes are working in the neurosciences, so if we have neuroscience ideas or neuroscientists with ideas, we raise these ideas, plans, and directions with scientists who have a knowledge base and the wisdom to go with it to make a decision. In the behavioral sciences we do the same thing. We try to bring scientists from all over together to talk about where the research enterprise is, where the new ideas are, where the activity is.

Mr. **Walgren**. How do you decide between the neurosciences and the behavioral scientists?

Dr. **Frazier**. Some of it, I guess, is political when you get right down to it. There are a lot of people with various and competing interests. Some of it is experience. I have been around about 45 years in the medical profession, and you develop an awareness of where things have been. I have seen 13 new treatments for schizophrenia, all of which have been unsuccessful, so I would say that you don't try to reinvent the wheel.

Part of it is a kind of intuitive, educated guess. Also, you know what is happening in the rest of the world so you don't try to duplicate or necessarily replicate what other people are doing. For example, what they are doing at the Karolinsky Institute in Sweden, we don't want to be entirely replicating at this time. Sometimes the decision is made because of staff input because a sophisticated staff tends to work very hard and research the area in depth, and also looks at the expertise, and the interested scientists who are available. It is not an easy decision.

Mr. **Walgren**. They say in cancer that one-third peer reviewed and recommended grants are not funded. How much is that in your area?

Dr. **Frazier**. We are a little bit higher than that since we don't have as big a pool of researchers. On the other hand, we are seeing an increasing number of sophisticated researchers, some of whom have worked in other institutes. I was going over the AIDS research applications yesterday, and I can tell you that there are very few psychiatrists doing research in AIDS, but a large number of other people are doing research on AIDS from the standpoint of the glialall immune system interaction in the brain. The development of AIDS research is an ideal example of the kind of behavioral input.

Mr. **Walgren**. AIDS has been around for a while, has it not?

Dr. **Frazier**. Yes, blood samples from 1971 from the Addiction Research Center at Lexington have been reviewed, and a number of those blood samples have tested positive for AIDS.

Mr. **Walgren**. So this is not new. I gather these new imaging mechanisms are very interesting because of their ability to identify chemistry in a nonevasive way. How does your budget react to that? Here is a new potential, something that I gather is not more than several years old, a great promise for a differentiating between people who have real tough symptoms versus a normal presentation.

How do you start to invest and drive that area?

Dr. **Frazier**. Essentially positron emission tomography, PET scanning, started at the NIMH with Dr. Louis Sokoloff. He developed the theory behind it. Then, with the collaboration of NIH and NIMH, along with former intramural—UCLA, UC-Irvine and a number of other places—the technology, and clinical, and research applications were developed. Gradually we have built a number of regionalized centers that offer the various imaging technologies.

The technology is not widespread, but certainly it is very productive in terms of research.

Mr. **Walgren**. That is sort of a relatively expensive area.

Dr. **Frazier**. Right.

Mr. **Walgren**. How do you factor that into your decision allocation? Do you sort of set aside a certain amount of your budget that you would like to see pursued in that area.

Dr. **Frazier**. It is not a specific set-aside, but it is an emphasis that we intend to evolve certain kinds of research enterprises and certain areas.

Mr. **Walgren**. Are you capped off by limitations of funds?

Dr. **Frazier**. Yes, we are. We have real problems. We also have the problem of infrastructure requirements and high technology that requires very expensive equipment. We have that problem even in the research centers where we are conducting fairly sophisticated research. We are not keeping up with their requirements on an annual basis for their obtaining the equipment available. I think this is a big policy issue that needs to be addressed.

Certainly, I don't think the cost of research is going to go down. I think as more and more high technology equipment comes on-line that we are going to find that the cost is going to keep going up. This equipment has a short life-span, as you know, because it needs to be replaced periodically. I think there needs to be a special kind of mechanism to address this issue.

Mr. **Walgren**. But let me ask you administratively in the NIMH, is there a mechanism for giving special emphasis to these imaging technologies, and how does that deal with the fact that apparently that area is very expensive and perhaps could consume all your money?

Dr. **Frazier**. We tend to this issue in increments and through the research center mechanism. The average NIMH research center grant is between $500,000 and $600,000 to a research center for equipment and for the maintenance of equipment or replacement of equipment and makes that equipment available to scientists on a shared basis. We also provide in every RO–1 or project grant an amount for equipment, though it is usually for smaller items.

However, we are seeing the average cost of grants go up this last year. It went up $4,000. When researchers can't buy equipment, they sometimes lease it, or when certain medical centers have equipment, they develop joint ventures to share it.

Any private sector involvement in this area has not been very much. Currently, 85 percent of the research effort in mental health, mental illnesses and addictive illnesses is supported by the Federal Government. Only 15 percent is provided by the philanthropic enterprises, the private sector. That is a serious problem. Only recently have we had industry to make some explorations relative to mental illness research. It hasn't developed in the same way as it has for cancers, as Paul Marks was talking about.

Mr. **Walgren**. Well, we certainly want to encourage you in every way, because I guess most feel that this will be an area where the progress will be really dramatic. You had mentioned earlier on, and I didn't—I'm sorry, I was only listening with one ear—you said something had peaked out, and that therefore we ought to be in a mode of sort of sitting back and watching and monitoring the directions of research?

Dr. **Frazier**. RO–1's, the efficacy of RO–1 driving the policy.

Mr. **Walgren**. I'm sorry. What are RO–1's?

Dr. **Frazier**. Field-initiated-research-project grants. We have had a quota on the number of RO–1's the Institute is to fund each year. The RO–1 quota essentially determines a great deal about the rising cost of each research grant. The RO–1 quota uses up more and more of the budget, so that the ability to bring together a cooperative research enterprise of varied mechanisms directed by major research universities or major research medical facilities is limited.

Mr. **Walgren**. Well, OK, thank you very much for being a resource to us, and we would like to develop that relationship between you and the task force in every way.

[Questions and answers for the record follow:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Alcohol, Drug Abuse, and
Mental Health Administration
Rockville MD 20857

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The Honorable Don Fuqua
Chairman, Committee on Science and Technology
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

Thank you for the opportunity to respond to the questions submitted by members of the Science Policy Task Force following the hearing held April 22-24, 1986, on "Policies for Biomedical Research." I regret the delay in my response. I will respond to your questions in the order in which they appeared in the letter.

1. It is generally recognized that federal support of biomedical research is important so that our institutions can address public health needs. However, with increasing budget constraints, funds must be used wisely so that the opportunity for public health benefit is maximized while maintaining our scientific and technical leadership. What criteria should the government consider in addressing this issue?

The goals of maximizing public health benefits and maintaining scientific and technical leadership complement each other and are mutually dependent. Advances in basic research are critical to progress in the prevention, control, and treatment of diseases. Despite this, the percentage of total health care dollars dedicated to health research has dropped over the last 20 years. For example, health research including basic biomedical, behavioral, and clinical research on public health problems has dropped from 2.8 percent in 1963 to 1.5 percent in 1983. To remain at the cutting edge of science and technology, the United States cannot afford to allocate such a small portion of the health dollar to research. In the basic biomedical and behavioral sciences, Federal health agencies attempt to obtain the best information on the need for funds in particular areas of basic research. We have found that one of the most valid techniques for estimating this need is the level of "effective field demand," that is, the cost of all proposals for research that meet the criteria of scientific excellence of the peer review system. In addition to scientific merit, allocation of funds to one or another specific public health problem or disorder also involves consideration of its magnitude or prevalence; its severity as measured by mortality rate, seriousness of the associated disability, duration or chronicity of the illness, or disruption of family life; and the costs of health care, the effects of third-party reimbursement mechanisms, and reduced productivity. A careful balance of each of these criteria from scientific merit to economic costs to society must form the basis of informed budget decisions.

2. What strategies are most effective in combatting disease and improving health and health care? When is this best done through understanding of the disease process? What has been the relative success of therapeutic or preventative strategies? Are there specific studies or data to address these questions? What should be the proper balance in overall research programs?

Obviously, the ideal strategy for combatting a disease is to prevent it from occurring. If successful, such a strategy would eliminate both the human suffering and the costs associated with treatment. However, given our lack of understanding of how to prevent most diseases and the fact that millions of individuals do suffer from hundreds of diseases, therapeutic strategies are of more immediate relevance and necessity. Fundamental to both the therapeutic and prevention strategies is an understanding of the disease process, its etiology, its course, and the risk factors associated with it. Thus, understanding the causal chain in a particular disease process provides a basis for adopting appropriate prevention and/or therapeutic strategies. Without such knowledge, effective prevention or treatment would be improbable. Therefore, I feel primary emphasis should be placed on basic and clinical research aimed at increasing our understanding of the health and disease states. Research on models and methods of prevention, treatment, and barriers to treatment are critical and should be given adequate support, but not at the cost of research on basic psychobiological processes underlying health and disease states.

3. How will present and future biomedical research and technologies impact on the cost of medical care? Who should bear the cost? What will be the overall consequences?

It is difficult to predict the impact of biomedical research and technology on costs because of the countervailing forces involved. It is likely that the cost of care for some disorders will decrease while the cost of care for other disorders may increase. Further developments in biomedical research may lead to the elimination of some illnesses, lower incidences of others, more effective treatments, more rapid recoveries, lower levels of resulting disabilities, and higher levels of productivity for health personnel. Biomedical research may also lead to costly treatments for previously untreatable conditions, increased incidence of some disorders by keeping more people alive longer, the development of complex and more costly diagnostic procedures, and the need for more advanced professional and technical training for treatment personnel. The overall result will be a higher quality and standard of care for more people across a wider distribution of disorders, but the long-term impact on costs is difficult to predict.

4. Is it possible to form a strategy leading to greater emphasis on the development of cost-saving research and technology in contrast to the rapid increase in health care costs as a result of the high technology used in current medical practice?

The technology used in current medical practice is expensive because it usually represents the state of the technical art, and has not yet benefited by cost savings of large volume production. Researchers and technicians attempting to solve a problem use the most advanced technology available. Cost of prototype technology is secondary to its ability to solve the problem. If the prototype technology solves the problem, it is usually marketed to the general medical community by private entrepreneurs. As the technology matures, its cost should follow the path of other technologies and decline. It would be possible to create a research and development program that focuses on the development of less expensive treatments and technologies, but this should not interfere with the process already in place. The development and use of a treatment or technology, even if expensive, allows for the possibility that further technological development will lead to its implementation or production at a lower price.

5. Is government targeting of research for certain health problems desirable? If so, what should be the balance between support of targeted versus non-directed programs? What criteria should be used in the decision-making process and who should be involved?

I believe that it is sometimes desirable and even necessary for the Government to target certain health problems for attention by the research community. However, such targeting should be done very conservatively, for sources of scientific progress are difficult, if not impossible, to predict and cannot be programmed with any certainty. In targeting a problem, the Government should limit itself to specifying the general goals desired and facilitating those goals, but not attempt to specify how the research should be done. Criteria for selecting targeted areas might include the magnitude and urgency of the public health need, the extent of the current effort, the potential for immediate payoff, the availability of funding and personnel, and the impact on other research endeavors. Targeted research programs should comprise a relatively small proportion of the total research effort. The balance of support should favor nondirected programs that conduct or support high-quality research aimed at expanding our biomedical and behavioral knowledge base. It is through the expansion of our general knowledge about psychobiological systems that we are more likely to develop an understanding of the malfunctions that lead to particular illnesses.

If you need additional information, please contact me. I am looking forward to reading the Science Policy Study Report.

Sincerely yours,

Shervert H. Frazier, M.D.
Director
National Institute of Mental Health

Mr. **Walgren**. Let's then turn to Dr. Fredrickson. It is good to see again, Dr. Fredrickson.

[A biographical sketch of Dr. Fredrickson follows:]

Dr. Donald Sharp Fredrickson

Present title: President, Chief Executive Officer, and Trustee, Howard Hughes Medical Institute, Bethesda, Md.

Birth: Canon City, Colorado, 1924

Education: B.S. University of Michigan, 1946; M.D. University of Michigan, 1949.

Postgraduate training: Peter Bent Brigham and Massachusetts General Hospitals; Harvard Medical School; and National Institutes of Health

Employment: 1984- : President, Howard Hughes Medical Institute;
1983–1984: Vice President, Howard Hughes Medical Institute;
1981–1983: Scholar-in-Residence, National Academy of Sciences;
1976–1981: Director, National Institutes of Health;
1975–1976: President, Institute of Medicine, National Academy of Sciences; and
1953–1974: National Institutes of Health, Scientist, Clinical Director, Director of Research and Director of the National Heart Institute.

Expertise: Basic laboratory and clinical research in the field of lipid metabolism and genetics; organization and conduct of science.

Other activities: Member, White House Science Council Member, National Academy of Sciences

STATEMENT OF DR. DONALD S. FREDRICKSON, PRESIDENT AND CHIEF EXECUTIVE OFFICER, HOWARD HUGHES MEDICAL INSTITUTE, BETHESDA, MD, AND FORMER DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Dr. **Fredrickson**. It is good to be back.

Mr. **Walgren**. Do you qualify as the only witness who has the money?

Dr. **Fredrickson**. There is never enough, Mr. Chairman.

Mr. **Walgren**. We are real happy to see any foundation involved in these areas and certainly the one that you are involved in, the Hughes Foundation. That may not be the exact name of it. The Howard Hughes Medical Institute can only be a real good thing to happen for our country, so let me ask you to tell us the things that you really would like to emphasis for the public record at this point, and in the interest of time, if I could suggest a 10- to 10-plus-minute range, that would be good, and then we can pursue things after. I apologize for being under time pressure, but I've got some other commitments on the other end that I am trying to meet.

Dr. **Fredrickson**. I'll just submit my full testimony for the record, Mr. Chairman, because I have to add that I am the man most responsible for the quota that Dr. Frazier was concerned about. Maybe I can come back to that.

Let me just make a couple of clarifying statements about the Howard Hughes Medical Institute. It is a medical research organization and not a private foundation under the statute, and that means that it carries out work primarily by employee scientists who work in laboratories that are staffed and equipped and paid for by the Institute. The organization is run by a central executive. It is helped a great deal by expert advisers from the outside, and it is responsible to a nine-member board of trustees.

Nevertheless, and that last description notwithstanding, all of our scientific activities are decentralized and largely conducted in academic centers and teaching hospitals. At each location, HHMI and the institution attempt to form a collaborative partnership sharing facilities and resources and permitting me a luxury that I never had when I was the Director of NIH, and that is paying attention to the whole institution to see what we might be able to do for it, rather than funding individual investigators.

Our experience with basic science is certainly no different in the private sector than you have had described by the experts this morning. One selects the best people, tries to support them well, but above all make certain that you preserve their autonomy, choice of subjects and their change of direction must be up to them, and to judge their achievement by peer review and not on the basis of the relevance of their discovery. I think that all our Federal agencies that you have heard from this morning supporting biomedical research clearly understand what is the nature of basic research, and they follow those same philosophies.

HHMI will spend more than $1 billion in the next 5 years on the support of science in four major areas: genetics, cell biology, immunology at present, and a new program in neuroscience. Most of our scientists are doing basic research, but some of them are in clinical locations, and we have a heavy emphasis on structural and molecular and cell biology.

The institutional reference that I referred to earlier is this: that as the Director of NIH one is unable to have much influence on the totality of the support of the Institutes or the institution because of the nature of the budget. There are 15 line item budgets, each sending their support to individuals in a variety of institutions, and I think that that is a desirable and necessary fragmentation of that kind of support. But it does prevent you, as the director of the whole enterprise, from paying attention to what impacts you are having with that kind of selecting funding on institutions.

That is particularly important today because the institutions are under a particular pressure for a variety reasons. One is that the progress in biology has been so rapid that they are required to transform their facilities to equip themselves with instruments and with kinds of people that they had not anticipated that they would need so rapidly in the past. It also puts great strain on the capacity of the institutions to integrate their activities so that they move in that desirable continuum from very basic science to clinical application.

Let me just touch upon a couple of points with reference to the materials that you sent out to us, Mr. Chairman. You ask about applied research, and as you are clearly aware, there is no easy dividing line between basic and applied research. I think the definition best rests on whether one wants to support inquiry or to procure a product. An agency like NIH has to work over the whole continuum. I think it seeks basic knowledge and practical applications in about the right ratio, and it should be continued to be encouraged to do so, but the agency is better adapted to basic research and certainly industry to apply.

I think that cooperation between the Federal and the academic and industrial research in biomedicine has come a long way in the past two decades, and very little of the disaster predicted when venture capital began to merge, or to support some activities in academia have actually occurred. Nevertheless, there are still mechanisms for improvement that are needed, and we are all seeking for the best compromise between the ambitions of those differently driven research enterprises.

It is interesting that we speak here in everyone's testimony of AIDS. I think AIDS is a case in point in this sense: that remarkable knowledge of the AIDS virus, including intimate details of its structure, has now been obtained in a rather remarkably short time. Now the biomedical research agencies in the Federal Government and industrial partners face a life-or-death challenge that will tell us how good our structure is. Can they take this knowledge and convert it to effective vaccines or medications, and how long will it take? I would guess that our success or failure in that particular enterprise may direct attempts to find new kinds of interstructures between basic and Federal laboratories and industry to see if we can mobilize to meet challenges which are of extraordinary kind of this sort.

Well, who sets the priorities, you ask? In HHMI, the program priorities are set by the scientific managers and advisers, and they are ratified by nonscientist trustees. I think, in the case of the Federal Research Agency, Congress has the role of trustee. The appropriation process, then, really essentially sets the program emphases, and I think in the case of where good technical advice is heeded, the system works reasonably well. Where priorities have to be set among different fields of scientists however, there is no effective system. I think the lack of a suitable balance for, and a forum for experts and trustees to review and to adjust the balance of overall R&D funding in the United States is a serious deficiency in our system.

Big science creates problems for all participants, however, and I have given you an example in my testimony relative to mapping of the human genome which may be one of the most exciting possibilities in biology in the next 20 years, how difficult it is going to be to organize that, and just to cheer you up, it is not due to the political process that this is going to be so difficult, or necessarily will the political process have the answer to it. It has got to come from the organization of science self.

You ask about the policies for infrastructure maintenance. I have addressed the fact that one advantage we have and used is that we can, at the time the scientists are mobilized to work in one of our units in affiliation with the universities, we can look at their total needs in order to bridge the activities of biology and to the other disciplines, and over the last few years we will have committed about $100 million in partnership with institutions to renovating and constructing new laboratories. We also have core laboratories and certain national facilities that supply all of biomedical science in certain areas. One example is the intended new port that we want to make possible on the light synchrotron at Brookhaven, which will serve not only Hughes' scientists, but the entire biomedical research community.

What about the availability of qualified scientific and technical personnel? Well, I think, as measured by the number of worthwhile projects that could be successfully mounted, biomedical science still suffers some very severe deficiencies in properly trained people in this country. Every medical research institution needs more skilled molecular and structural biologists. Many medical schools need specialists in infectious disease and immunology and other fields that are impacted by new opportunities for the application of research funding. There is a particular difficulty, as you have heard today, in attracting that small, but essential fraction of medical school students, graduates into research-oriented careers. HHMI has just taken a small step in this direction. It has now a partnership with the NIH, with a Federal agency in which we have undertaken to create a center at the NIH, taken the old convent and converted it into an educational center, and added a residence to it. Very soon there will be living there a community of medical students chosen from across the country who will be allowed to have a year of time in an NIH laboratory to try for themselves the opportunities and the meaning of science as a possible career choice.

With that, I think that summarizes very briefly the aspects of HHMI that I think are most important for your record. I'll be glad to answer any other questions if you have them.

[The prepared statement of Dr. Fredrickson follows:]

2058f

Opening Statement: Testimony before
House Committee on Science and Technology
April 23, 1986

Mr. Chairman:

I am Dr. Donald S. Fredrickson, president of the Howard Hughes Medical Institute. I had the pleasure of appearing before this Committee, as director of NIH between 1976 and 1981. It's good to be back, and to speak this time from the private sector.

I have been requested to describe the Institute and respond to some of the questions raised in the Committee's statement of purpose concerning the management of Federal biomedical research programs.

Description of HHMI. The Howard Hughes Medical Institute is a medical research organization. In keeping with the definitions of such an organization in the Internal Revenue Code and applicable Treasury Regulations, our principal activity is the direct conduct of medical research in conjunction with hospitals. Most of the scientific activities of HHMI are performed by employee scientists and trainees who work in laboratories staffed, equipped, and maintained by the Institute.

HHMI was founded in 1953 and reorganized in 1984 under a new Board of Trustees. The sale last year of our sole asset, the Hughes Aircraft Company, created an endowment of approximately $5 billion. This has been invested so as to maintain its real value in perpetuity and provide a stable return to be spent in accordance with the chartered purpose of the

Institute: to promote human knowledge in the basic sciences, principally in the field of medical research and medical education.

HHMI expects to spend more than a billion dollars in the next five years for this purpose, and is thus in a position to strengthen and help preserve the balance of a national system for advancing the knowledge of biology and its application to health. The Institute must also be sensitive to the effects its operations may have upon the individual institutions where it is present and where it is not. Its operations are designed to complement those of the other private and public organizations dedicated to the same cause.

HHMI is governed, and its program determined, by a central executive body responsible to a nine-member Board of Trustees. The scientific activities are decentralized and largely conducted in academic medical centers and their teaching hospitals. At each location, HHMI and the host institution have established a collaborative partnership sharing facilities and resources. Each HHMI scientist is a member of the institutional faculty as well as the Institute staff.

Policies for Support of Basic Research. The HHMI program is dedicated mainly to basic research, usually in a laboratory, sometimes in a clinical setting. There is strong emphasis on structural, molecular, and cell biology. The work in these disciplines is not focused on specific medical conditions, but rather on life processes that underlie many aspects of health and disease.

HHMI research is presently divided into four programs characterized by rapid advance: genetics, immunology, metabolic regulation, and neurobiology. We believe the policies essential to meet our objectives are common to all basic science. One selects the best people, sees that they are properly equipped, and promotes a maximum of interaction and informational exchange among fields. Above all, one protects the scientists' autonomy and judges progress by peer review.

I reemphasize these last two conditions. Professional scientists must be accorded certain kinds of independence that both define and sanction their role as contributors to the accumulation of intellectual capital upon which society depends. The scientists must be autonomous in selecting the approach to their work and free to shift to new, more promising lines of inquiry. Relevance of the work to some practical objective does not determine the right to proceed. The quality of the scientists' work must be judged by their scientific peers. Of course, the research must conform to the law and the rules of the host institution or hospital. If not, the independence of the scientist must yield.

In the biomedical area, the major source of support for basic science has to come from federal agencies, principally NIH and NSF. The policies of those agencies must, and do, incorporate the principles I have just described.

Applied Research. There is no easy dividing line between basic and applied research. The definition best rests on whether the objective is to support inquiry or to procure a product. An agency like NIH supports research over a broad continuum, seeking basic knowledge and practical applications. It should be encouraged to do so. But the agency is best adapted to basic research, and industry to applied.

Cooperation between Federal, academic, and industrial research in biomedicine has come a long way in the past two decades, but mechanisms for improvement are needed. The problem of AIDS is a case in point. Remarkable knowledge of the AIDS virus, including intimate details of its structure, has been acquired. Now the biomedical research agencies and their industrial partners face a life-and-death challenge. Can they convert this knowledge to an effective vaccine or medication, and how soon?

Who Sets the Priorities? In HHMI, program priorities are recommended by scientific managers and advisors and ratified by nonscientist Trustees. In the case of Federal research agencies, Congress has the role of trustee. Here the appropriation process essentially sets program emphasis. When good technical advice is heeded, the system works reasonably well. However, when priorities must be set among different fields of science, there is no effective system. Lack of a suitable forum for experts and trustees to review and adjust the balance of overall R & D funding is a serious deficiency in our system.

Big Science creates problems for all participants. All the difficulties cannot be attributed to Congress or the Executive Branch. Let me cite one present-day example. It is generally agreed that the human genome--the 100,000 or so genes of each individual--will eventually be located on one or another of the 46 chromosomes. If the precise structure of every gene were to be determined the secrets of cancer and many other diseases could be much closer to hand. The necessary technology is available, but the task is formidable. It would cost billions of dollars and require the dedication of many experts to a somewhat pedestrian task for years.

At least three Federal agencies have a keen interest in such a project: NIH, DOE, and NSF. There is also some commercial interest, though the question of financial gain limits enthusiasm. HHMI wishes strongly to play a helpful role. Some of our scientists are developing probes to locate mutant genes underlying human disease, and we also maintain the principal gene map. The possible sequencing of the human genome interests geneticists all over the world. The unresolved problem is how to attain the necessary cooperation on the scale required. I do not cite this example to suggest need for Congressional intervention, but rather to point out that all problems in the realm of science cannot be attributed or addressed to the political process.

What Are the Policies for Infrastructure Maintenance? It is generally agreed that the structure and equipment of many American institutions where biomedical research is conducted, and where scientists and medical students are educated, are substandard and growing worse. Part of the solution will have to come through enhanced Federal appropriations. There is a also a role for industry and private-sector agencies.

The HHMI-university collaboration is designed to have a favorable impact on the institutional partner. It seeks to strengthen the infrastructure and the common milieu for research. These last four years, HHMI will have made capital investments for construction or renovation of laboratories amounting to more than $100 million. Our core laboratories and certain national facilities provide sophisticated technological support not only to HHMI scientists and their institutional colleagues, but to the entire biomedical research community.

Availability of Qualified Scientific and Technical Personnel. As measured by the worthwhile projects that could be successfully mounted, biomedical science suffers severe deficiencies in properly trained personnel. Every medical research institution could use more skilled molecular and structural biologists. Many medical schools need specialists in infectious disease, immunology, and other fields impacted most by new opportunities for application of research findings. There is particular difficulty in attracting that small but essential fraction of medical students into research-oriented careers.

HHMI has made one of its partnership agreements with NIH to maintain a research training program for medical students, usually at the end of their second year. Working with skilled preceptors in the excellent NIH laboratories, they will gain a solid exposure to research for up to a year. Moreover, the Institute is spending more than $10 million over the next five years to build a student residence and refurbish an old convent on the NIH grounds for an educational center. This HHMI-NIH Research Scholars Program, familiarly called the "Cloister Project," is taking place at NIH's Mary Woodard Lasker Center for Science and Education. Thirty-eight students from twenty-one medical schools across the country have been selected to join the 1987 class.

Involvement in Broad Research Programs. Each HHMI scientist is linked to a network that provides continuing communication with colleagues in the same general field. Scientists' conferences and workshops in each of the major program sectors are regular events. Disciplines are also mixed to enhance cross-fertilization. In their home laboratories, HHMI scientists work side by side with university colleagues, and maximum integration within the academic community is encouraged. Each HHMI scientist is expected to participate in the activities of the hospital or university and may allot up to a quarter of his or her time to teaching or other duties, except heavy administrative chores that distract from research.

Support by Federal agencies of scientific interactions involving multiple institutions has been steadily increasing. This has been particularly true in the more applied research. The roles of NIH in carrying out clinical trials and evaluation of technology have earned worldwide respect.

HHMI has no formal affiliations with foreign institutions, though its scientists frequently collaborate with their counterparts abroad. Federal agencies have been very active in promoting such interactions. Among the 87 NIH grantees who have received Nobel prizes, a significant number were foreigners. I believe the provision of support and frequent interactions with the best of world science is both appropriate and necessary for American Federal science agencies.

Mr. Chairman, I will be pleased to answer any questions.

DISCUSSION

Mr. **Fuqua**. Thank you, Dr. Fredrickson. I apologize for having to be in and out over the years, it is difficult to be in two places at one time.

Dr. **Fredrickson**. I do understand your predicament.

Mr. **Fuqua**. The latter part that you mentioned about the joint venture with NIH and Hughes, is this a prototype that you might do in other places if this develops very well?

Dr. **Fredrickson**. Yes, I think that is quite possible, Mr. Fuqua. The idea is to, first of all, provide students with a salary so they don't go further in debt; to permit them to have a good period of time at a critical moment in their careers—between their second and third years of medical school; to give them the opportunities to go into the best labs and work on problems and see what the method is like, what this kind of life could be.

There is also another very important feature of it, we think. They need to do this in a community. They need to share their experience with science, and people who do science, so that they can learn together the essential disciplines and the absolutely essential issues of discipline and ethic that are required for successful pursuit of science.

If it works at NIH and the Cloister, we can see that happening, perhaps, in one or two other locations around the country. We are going to have 38 students from 21 institutions in our next class. We would like to see if maybe that would be useful to try in other parts around the country. So this is the prototype. We will see how it works.

Mr. **Fuqua**. It sounds like a very exciting program.

Dr. **Fredrickson**. The students are very excited about it.

Mr. **Fuqua**. I'm sure they would be. It sounds like you have a very good broad cross-section.

Dr. **Fredrickson**. Yes, and it was deliberately intended to be as broad as we can make it.

Mr. **Fuqua**. In the scientific program managers within Hughes, and you say they are responsible to the board of trustees, I believe.

Dr. **Fredrickson**. Yes.

Mr. **Fuqua**. How do they interreact in trying to establish their priorities, and do they serve on a rotating basis, or are they more permanent people? How much flexibility do you have in setting priority?

Dr. **Fredrickson**. We have a lot of flexibility in our advisory apparatus. We have a small group of scientific managers. We are as lean as we can be, but we have a good medical advisory board of about 10 people who serve on rotation 5-year terms from around the best scientists in the country we can get, and then a scientific review board below that for each of the four programs, and they rotate and continue to interact on a regular basis.

Each of our scientists that we hire must be recommended by the medical advisory board. We don't like to let them vote because we don't want to get arithmetic, but the consensus has to be there. They are there to choose excellence, and they are responsible in a great deal for the quality of judgments. They are a sounding board. The scientific managers have to establish a certain programs they would like to test, and I think basically they are primarily—the scientific people are responsible for the priorities.

One must, then, pass those through the trustees of Hughes who are very interested in large commitments of resources, of course, for construction or for the nature of programs that we may intend to implement. They don't pretend to judge the particular individual projects or the instruments that we have but, but they want to know what we are doing and what is the global perspective. I think that is very helpful to have that largely nonscientific, but informed educated people who are genuinely curious, and ultimately responsible for what is the total effect is going to be.

Mr. **Fuqua**. Does your board of trustees—and maybe you haven't had enough experience with them so far—say, "Dr. Fredrickson, we think we ought to spend more money in cancer research than we are doing in heart right now or more in allergies similar to what Congress has done over the years to NIH"?

Dr. **Fredrickson**. No, they don't, Mr. Chairman, and there are a couple of reasons for that. We are not disease-oriented. We are deliberately not directed at a given disease. We are underwriting research in the basic disciplines that will probably affect all aspects of health and disease, and thus far they have not attempted to push us in one direction or another, but they have made us prove to them our arguments for why would we go in this direction. Why put $60 million in structural biology and x-ray crystallography at major institutions across the country? Why do that, as opposed to other things?

So I think that is an important mechanism. Make the experts prove their point, but let them have a chance to first bring up the priorities.

Mr. **Fuqua**. Do you still use the peer review system that is in effect at NIH, or do you look at alternatives?

Dr. **Fredrickson**. No, you have got to use peer review in basic science, Mr. Chairman, there is no other way around it. But we do have a luxury that NIH has not been able to afford. We choose people on the basis of what their overall record has been rather than their immediate proposals.

Now when young people come, that is somewhat more difficult, but the references we use, we judge for ourselves. We don't ask them what specifically they want to work on.

Mr. **Fuqua** It is like a young investigators program?

Dr. **Fredrickson**. Yes, we don't judge by the proposal. We judge by the performance over a period of time, which fortunately we can extend 5 to 7 years in the instance of many investigators.

Mr. **Fuqua**. Your time hasn't run out, but mine is. I've got to go vote. I thank you very much for being here this morning. It has been very helpful.

Dr. **Fredrickson**. It was good to be back.

[Whereupon, at 12:45 p.m., the task force adjourned to reconvene on Thursday, April 24, 1986, at 10 a.m.]

POLICIES FOR BIOMEDICAL RESEARCH

THURSDAY, APRIL 24, 1986

House of Representatives,
Committee on Science and Technology,
Task Force on Science Policy,
Washington, DC.

The task force met, pursuant to notice, at 10 a.m., in room 2318, Rayburn House Office Building, Hon. Doug Walgren (acting chairman of the task force) presiding.

Mr. Walgren. Let me welcome you to this third day of exploration in the biomedical research area by the task force of the Committee on Science and Technology in this study which we are trying to put together in these months.

During the previous 2 days we have had testimony on the direction of Federal research programs at National Institutes of Health, the National Institute of Mental Health and Veterans' Administration, and a number of scientists and universities and private research institutes giving us their perspectives on the value and the directions which we ought to pursue. They have clearly underlined the importance, if we are to maintain the U.S. scientific equality in the world consistent with stable funding for qualified projects, particularly as judged and selected by the peer review process, and for clearly full and adequate training support for young basic researchers, both scientists and physicists.

The benefits of the U.S. biomedical research effort were also underlined and the application of basic information to the development of both health technology, and improved health care and improved public health conditions are clear and evident. This morning we want to consider future directions for Government policy in support of biomedical research and ask how the Congress and scientists and other contributors to this area can best promote these goals in the future.

We have a long list of six or so particularly distinguished witnesses. We have Dr. Paul Berg, a Nobel Prize winner and Willson professor of biochemistry, as well as the director of the center for molecular and genetic medicine at Stanford University; Dr. Frank Young, Commissioner, Food and Drug Administration; Dr. Donald D. Brown, director, department of embryology, Carnegie Institution of Washington, and in addition, involved in the Life Sciences Research Foundation; Dr. William Neaves, dean, graduate school of biomedical sciences, University of Texas Health Science Center; Dr. Alexander Mac Lachlan, senior vice president—technology, E.I. du Pont de Nemours & Co. We also have Dr. Albert Williams, director, health sciences program, the Rand Corp.

We certainly appreciate all of you, particularly in view of your past accomplishments and standing that you have in these various disciplines, being a resource to us, and we appreciate your coming and talking with us about your perspectives and guidance that you would like to see the system give consideration to.

I would like to say at the outset that your written statements and comments will be made part of the record, and you can feel free to focus on parts or underscore in any way that you feel most effective, those points that really deserve to be focused on. Since we do have six witnesses, obviously if we are to get through in 2 hours or so, in consideration of other witnesses and some thoughts we might exchange after your testimony, I would ask you to keep somewhat limited in the time that you take for the initial presentation.

So with that, let me call first Dr. Berg. As I said, Dr. Berg is both a Nobel Laureate but also a professor of biochemistry at Stanford University, and we are very pleased you could join us, Dr. Berg. Please go ahead and tell us some of your perspective in whatever way you feel you would like.

[A biographical sketch of Dr. Berg follows:]

DR. PAUL BERG

Date and Place of Birth. June 30, 1926, New York, New York.

Education. B.S., Pennsylvania State University, 1948; Ph.D., Western Reserve University, 1952.

Professional Background. 1950-1952—Predoctoral Research Fellow, National Institute of Health; 1952-1954—Postdoctoral Research Fellow, American Cancer Society, Dr. H.M. Kalckar, Institute of Cytophysiology, Copenhagen, Denmark and Dr. Arthur Kornberg, Washington University, School of Medicine; St. Louis, Missouri; 1954—Scholar in Cancer Research, American Cancer Society, Department of Microbiology, Washington University, School of Medicine; 1955-59—Assistant to Associate Professor of Microbiology, Washington University, School of Medicine; 1959-1960—Associate Professor of Biochemistry Stanford University, School of Medicine; 1960—Professor, Department of Biochemistry, Stanford University, School of Medicine; 1969-74—Chairman, Department of Biochemistry, Stanford University, School of Medicine; 1970—Named Sam, Lulu and Jack Willson Professor of Biochemistry; 1973-1983 Non-Resident Fellow of Salk Institute.

Honors. 1959—Eli Lilly Award in Biochemistry; 1963 California Scientist of the Year; 1966—National Academy of Sciences; 1966—American Academy of Arts and Sciences; 1969, 1972—Henry J. Kaiser Award for Excellence in Teaching at Stanford University School of Medicine; 1972—Distinguished Alumnus Award, Pennsylvania State University; V.D. Mattia Prize of the Roche Institute for Molecular Biology; 1974—Institute of Medicine, National Academy of Sciences; 1975—President, American Society of Biological Chemists; 1978—Honorary D.Sc., University of Rochester and Yale University; Elected Foreign Member, Japan Biochemical Society; 1979—Sarasota Medical Awards for Achievement and Excellence; 1980—Annual Award of the Gairdner Foundation, Nobel Award in Chemistry, Albert Lasker Basic Medical Research Award, New York Academy of Sciences; 1982—American Association for the Advancement of Science Scientific Freedom and Responsibility Award; 1983—National Medal of Science, Elected to American Philosophical Society; 1984—Elected Associate Member of EMBO.

Special lectureships. 1972—Harvey Lecture; 1977—Lynen Lecture; 1977—Weizmann Institute Lectures; 1978—Distinguished Lectures, University of Pittsburgh; 1978—Priestly Lectures—Pennsylvania State University; 1978—Shell Lecture University of California at Davis; 1979—Dreyfus Distinguished Lectures Northwestern University; 1980—Jesup Lectures Columbia University; Karl-August-Forster Lecture, University of Mainz, West Germany; David Rivett Memorial Lecture, CSIRO Melbourne Australia 1981—Charleton Lecturer, Tufts University School of Medicine; 1981—Truman Wesley Collins Lecture, Portland, Oregon; 1981—O'Hara Lecturer; in Molecular Biology, University of Texas, Dallas; 1981—Shaffer Lecturer, Washington University in St. Louis; 1982—Fred Smith Memorial Lecture, University of Minnesota; 1982—Smith, Kline & French Distinguished Lecturer UCSF; 1982—Joseph Henry Science Lecture; 1982—Wiley Jones Distinguished Lecturer, Rochester Institute of Technology; 1983—Robbins Lectures at Pomona College; 1984—William H. Stein Memorial Lecture, Rockefeller University; 1984—Smith, Kline & French Lecturer, Temple University; 1984—Gamow Lecture, University of Colorado; 1984—Halsell Lecture, San Antonio, Texas; 1984—Mautner Memorial Lecture; 1984—Charles E. Dohme Memorial Lecture, Johns Hopkins University; 1984—Mert Utter Lecture, Case Western Reserve; 1984—Weizmann Institute of Science Jubilee Lecture; 1985—University of Houston Nobel Prize Winners Series.

Special Appointments. 1959-68—Editor, *Biochemical and Biophysical Communications*; 1966-69—Member of NIH Study Section on Physiological Chemistry; *Journal of Molecular Biology* Editorial Board; 1970-1980—Member of Board of Scientific Advisors of Jane Coffin Childs Foundation for Medical Research; Advisory Boards to National Institutes of Health, American Cancer Society National Science Foundation, Massachusetts Institute of Technology, and Harvard University; 1979—Elected to the Council of National Academy of Sciences and to the Scientific Advisory Board of the Welch Foundation; 1980, Appointed to the Editorial Board of the proceedings of NAS; 1984, Chairman, Whitehead Institute Scientific Advisory Committee, International Advisory Board of the Basel Institute of Immunology.

STATEMENT OF DR. PAUL BERG, WILLSON PROFESSOR OF BIOCHEMISTRY, AND DIRECTOR, CENTER FOR MOLECULAR AND GENETIC MEDICINE, STANFORD UNIVERSITY SCHOOL OF MEDICINE, STANFORD, CA

Dr. Berg. Mr. Walgren and members of the committee, I appreciate your invitation to participate in this inquiry and to the present status of biomedical science in the country. Particularly, I value the opportunity to discuss what directions the Government-science relationship should take in the future.

If the hearings of the last 2 days have conveyed a sense of pride in the remarkable achievements of the biomedical research enterprise during the past four decades and particularly during the last 15 years, then you also could not have missed our grave concerns and pessimism about the future. The decisions being debated now can topple American science from its acknowledged lofty position or it can make that preeminence unassailable for years to come.

The Government's investment in biomedical research has paid off handsomely. I notice that is the title of Don Brown's talk. I will allow him to go into more detail about how handsomely. I suspect that, dollar-for-dollar, it is probably the soundest and most rewarding expenditure of public funds made during that period. The most arcane forms of basic research were supported even when its applicability to human health could only be take on faith. Moreover, it did so with a system that relied on the judgment of peers to recognize outstanding and valuable contributions and research proposals rather than judging the merit of requests of political, geographic or other irrelevant criteria. Top-quality science will not flourish here or anywhere unless the judgment of quality is made by practicing scientific peers.

Why has the United States achieved such preeminence in the biomedical sciences? Much of the success of the biomedical sciences stemmed from the recognition by successive governments that the creation of modern facilities with state-of-the-art equipment, was met by farsighted programs for capital costs of construction, renovation and equipment.

The establishment of graduate and postgraduate training programs attracted our brightest and most promising talented young scientists into biomedical careers. The challenge was exciting, there were new barriers to be breached, there was financial support during the long and arduous training, and the promise of an independent research career for those of proven merit. The top echelon of American sciences were trained in one or another such programs. My own graduate and post-doctoral training was supported by National Institutes of Health training grants. With those not available I would probably have ended up compounding new coffee blends and soup mixes in the food industry. Thus, the system provided for its growth and renewal—new people with fresh ideas were drawn into the field and updated facilities created a situation where ideas, and not space and equipment, were the limiting factors to progress. Participants in this venture were imbued with the confidence that a mix of basic, applicable and clinical research would enlarge our intellectual horizons and lead to a deeper understanding of health and disease. There was no doubting that such a commitment would improve the vitality and health of our citizens.

However, I did not come to sing the praises of past achievements. My eagerness to testify reflects a deepseated concern that our current policies are threatening the long-term vitality, and even the viability, of the world's most successful biomedical research enterprise. Specifically, what are my concerns? First, I am alarmed at an attitude that research and discovery can be bought on short notice like commodities. However, scientific progress cannot be put on hold, nor can it be stockpiled like grain in silos or oil in deep salt caverns. Creating the research organization we now have took nearly half a century, a very substantial investment in wisdom, and a tenacious commitment to excellence. Its success to date has been brilliant; its promise for the future is, in my view, staggering, considering the opportunities that lie before us. Shall we reap the benefits, exploit the initiatives, or shall we put the system on hold? I think the choice is obvious.

Like all good investments, timing is critical and opportunities spurned or ignored may be lost forever or seized by others. Research groups are fragile and once disbanded they are not easily reassembled; inevitably such starts and stops—lurching—is wasteful of money and talent. From my perspective, I see a Government policy that is hovering on retrenchment; it has already severely eliminated capital investment in physical plants and equipment, and it now seeks to economize by squandering trained manpower. The policy I perceive will weaken, rather than strengthen, university-based research. By what measure of logic can we be considering a restructuring of Government science relationships when its past successes place it on the verge of major breakthroughs in medicine, industry and agriculture? And especially when that restructuring threatens to damage or impede the realization of achieving those breakthroughs.

What is the proper form for our investment for the future? One of the desperate needs for science to continue to be productive is the modernization of research facilities and equipment. Capital costs for new research facilities have not been available from the Federal Government for nearly ten years except by politically manipulated, and noncompetitive mechanisms. As a consequence, the most advanced forms of science are being done in aging and overcrowded facilities and with largely obsolete instrumentation and equipment. Surprisingly, this is true even in the major research institutions that have been most successful in receiving research grant support.

I hope the Congress and the executive branch takes note of a recently published White House Science Council report on "The Health of U.S. Universities and Colleges." In it, the committee, chaired by Mr. David Packard, acknowledges this serious deficiency and the dangers it poses. They proposed that a new fund be established in the National Science Foundation for each of the next ten years to which the universities can submit proposals. Moneys would be awarded on the basis of peer review, based on merit, and would have to be matched by non-Federal funds. That report pointed out that the Government's $100 billion R&D budget is for military research, $8 billion for universities, and that very little of that research is relevant to strengthening the basic science in this country. Even under conditions of reduced funding, a small shift in this ratio would greatly strengthen the universities, and, in the long run, such a redistribution would, I believe, also strengthen the military.

The advancement of science, more than any other intellectual activity, requires talented young people. But the talk now is that the previously successful modes of attracting and training the next generation of biomedical scientists is at risk and may be terminated or drastically reduced. That would be a blunder. Young scientists in training are the very heart of our research teams; indeed, it is students and not their professors who actually perform the experiments and, in many cases, generate the ideas that ultimately gain their mentors prestigious awards. There is no backing away from the need to select the next generation of scientists on the basis of merit. To attract the talented rookie we need to provide them with stable support for 4 to 6 years of research training and 2 to 3 years of advanced post-graduate training. I hope that your hearings will find a way to meet this necessity. For without a steady flow of fresh, inspired, ambitious young scientists, the quality and productivity of even the best research groups will decline.

I shall make a special plea for another rare type of individual—the physician/scientist—those who by training and bent, focus on basic biological problems related to human physiology and disease. Their double-barreled expertise is especially needed if we are to successfully apply the powerful methodologies developed during the past few years for understanding the molecular and genetic basis of disease. Presently, the Medical Scientist Training Program meets some of that need, but it, too, is in jeopardy of being eliminated along with other training programs. If anything, this program should be expanded so as to facilitate the transfer of knowledge and techniques from the bench to the bedside.

The achievements made during the last 15 years have already vindicated the judgment to support untargeted research in molecular biology, genetics. From it emerged an extremely powerful paradigm for analyzing the mechanisms of disease at a level no one would have thought possible in our lifetime. This has brought us to a new frontier, one which permits a more rational approach to the prevention and treatment of disease in a more rational way.

I have provided you with a list of crippling or lethal diseases that can now be analyzed at the molecular and genetic level, and as a consequence, our efforts for their prevention and cure can proceed on a solid footing rather than by guesswork. I won't expand on those diseases and leave them for the record.

At Stanford, we are presently developing a Center for Molecular and Genetic medicine. Its purpose is to expand our abilities and efforts to advance the basic science in a milieu of physician/scientists. Their aim is to explore the potential of the new breakthroughs in basic science in various areas of medicine. Similar developments are proceeding at several of our research institutions, but in each case their establishment and success will depend upon Government policies for support for construction, renovation, equipment and talent.

Does industrial support provide an alternative or supplement to Federal programs? I am afraid not, although there are some interesting attempts to find a way to help. First of all, the corporate culture is geared to short-term results and proprietary ownership. Both are the antithesis for the kind of stable support that projects with no immediate applicability or payoff require. I cite as an example of my argument the question—where was industry in the 1950's and 1960's when much of the groundwork for the biological revolution was laid? As they could not foresee how support of research on bacteriophage and E. coli and its enzymes could possibly pay off, they had little or no part in it, and in retrospect, that is where the ideas, the methods, the people that create our biotechnology industry emerged from.

Recently I was to remind President Mitterrand of France, that an institute in Paris, the Pasteur Institute, literally trained our generation of bioscientists who made the biotechnology revolution. The occasion was a trip when he came to Stanford to visit to find out how Stanford and the local industry were able to create this wonder of Silicon Valley and biotechnology. In fact, it has started in his own backyard. He was unaware, nor was anyone there aware of it.

Now, if industry missed it in the fifties and sixties, can we expect them to be any wiser in identifying the sources of the next biological revolution? Is it in developmental biology or neurobiology or some as yet unopened lead in molecular structure analysis? I do not see industry as being prepared to invest heavily in the health of the research enterprise, particularly when the information that is to be gleaned will be available to its competitors as well as to themselves.

I do not believe it is reasonable for this Nation to rely wholly on industry to support basic research. They can provide special kinds of assistance, but it is unrealistic to expect that the basic biomedical science enterprise could flourish or even survive from the sponsorship alone. Again, the Packard committee made a useful recommendation. They proposed that industry be granted tax credits commensurate with their support of university research programs, servicing equipment and of merit based scholarship programs.

Mr. Chairman, I have given you my frank views, and I am prepared to answer questions or respond to your comments.

[The prepared statement of Dr. Berg follows:]

TESTIMONY BEFORE COMMITTEE ON SCIENCE AND TECHNOLOGY

My name is Paul Berg and I'm presently Willson Professor of Biochemistry and Director of the Center for Molecular and Genetic Medicine at Stanford University School of Medicine. A curriculum vitae is attached to provide you with a more complete description of my background.

Chairman Fuqua and members of the Science Policy Task Force: Thank you for your invitation to participate in this inquiry into the present state of biomedical science in this country. I particularly value the opportunity to discuss what directions the Government-Science relationship should take in the future.

If the hearings of the last two days have conveyed a sense of pride in the remarkable achievements of the biomedical research enterprise during the past four decades, and particularly during the last fifteen years, then you also could not have missed our grave concerns and pessimisim about the future. The decisions being debated now can topple American science from its acknowledged lofty position or it can make that preeminence unassailable for years to come.

The government's investment in biomedical research has paid off handsomely. I suspect that dollar for dollar it is probably the soundest and most rewarding expenditure of public funds made during that period. The most arcane forms of basic research were supported even when its applicability to human health could only be taken on faith. Moreover, it did so with a system that relied on the judgment of peers to recognize outstanding and valuable contributions and research proposals, rather than judging their merit on political, geographic or other irrelevant criteria. Top quality science will not flourish here or anywhere unless the judgment of quality is made by practicing scientific peers.

Why has the United States achieved such preeminence in the biomedical sciences? Much of it, I believe, stems from the actions by successive governments to create modern facilities with state of the art equipment as well as to provide for a constant infusion of fresh talent to maintain a front-rank research enterprise. The need for state of the art facilities and equipment was met by farsighted programs for capital costs of construction, renovation, and equipment. The establishment of graduate and post-graduate training programs attracted our brightest and most promising talented young scientists into biomedical careers. The challenge was exciting, there were new barriers to be breached, there was financial support during the long and arduous training and the promise of an independent research career for those of proven merit. The top echelons of American science were trained in one or another of such programs. As a personal note, I should point out that my own graduate and post-doctoral training was supported by NIH fellowships; were those not available I probably would have ended up compounding new coffee blends and soup mixes in the food industry.

Thus, the system provided for its growth and renewal: new people with fresh ideas were drawn into the field and updated facilities permitted ideas, and not space and equipment, to be the limiting factors to progress. Participants in this venture were imbued with the confidence that the mix of basic, applicable and clinical research would enlarge our intellectual horizons and lead to a deeper understanding of health and disease. There was no doubting that such a commitment would improve the vitality and health of our citizens.

However, I did not come to sing the praises of past achievements. My eagerness to testify reflects a deep seated concern that our current policies are threatening the long term vitality and even the viability of the world's most successful biomedical research enterprise. Specifically, what are my concerns? First, I am alarmed by the spreading attitude that research and discovery can be bought on short notice like commodities. However, I assure you that scientific progress cannot be put on hold, nor can it be stockpiled like grain in silos or oil in deep salt caverns. Creating the research organization we now have took nearly half a century, a very substantial investment, wisdom, and a tenacious commitment to excellence. Its success to date has been brilliant - its promise for the future is, in my view, staggering considering the opportunities that lie before us. Shall we reap the benefits, exploit the initiatives, or shall we put the system on hold? I think the choice is obvious.

Like all good investments, timing is critical and opportunities spurned or ignored may be lost forever or seized by others. Research groups are fragile and once disbanded they are not easily reassembled; inevitably such start and stops, - lurching - is wasteful of money and talent. Our present government policy seems to be hovering on retrenchment; it has already severely limited capital investment in physical plants and equipment, and it now seeks to economize by squandering trained manpower. Such a policy is guaranteed to weaken rather than strengthen university-based research. I find it astonishing that we are considering a restructuring of government-science relationships when we are on the verge of major breakthroughs in medicine, industry and agriculture. More astonishing is the fact that such a restructuring threatens to damage or impede the realization of those breakthroughs.

What is the proper form for our investment for the future? If science is to continue to be productive it desperately needs a modernization of research facilities and equipment. Capital costs for new research facilities have not been available from the Federal government for nearly ten years except by politically manipulated, and non-competetive mechanisms. As a consequence, a surprising amount of the most advanced forms of science are being done in aging and overcrowded facilities and with largely obsolete instrumentation and equipment. Surprisingly, this is true even in the major research institutions that have been most successful in receiving research grant support.

I hope the Congress and the Executive branch takes note of a recently published White House Science Council report on "The Health of U.S. Universities and Colleges". In it, the committee chaired by Mr. David Packard, acknowledges this serious deficiency and the dangers it poses. To head off that danger they proposed that a fund be established in the National Science Foundation for the purpose of upgrading the research facilities of American universities over the next 10 years. Monies would be awarded to university proposals on the basis of merit determined by peer review and would have to be matched by non-federal funds. Where would the money come from? That report pointed out that the Government's $100 billion R & D budget is primarily for military research ($8 billion to universities) and that very little of that research is relevant to strengthening the basic science in this country. Even under conditions of reduced funding, a small shift in this ratio would greatly strengthen the universities, and, in the long run, such a redistribution would, I believe, also strengthen the military.

The advancement of science, more than any other intellectual activity, requires talented young people. But the talk now is that the previously successful modes of attracting and training the next generation of biomedical scientists are at risk and may be terminated or drastically reduced. That would be a blunder. Young scientists in training are the very heart of our research teams; indeed, it is students and not their professors who actually perform the experiments and, in many cases, generate the ideas that ultimately gain their mentors prestigious awards. There is no backing away from the need to select the next generation of scientists on the basis of merit. To attract the talented rookie we need to provide them with stable support for 4-6 years of research training and 2-3 years of advanced post graduate training. I hope that your hearings will find a way to meet this necessity. For without a steady flow of fresh, inspired, ambitious young scientists, the quality and productivity of even the best research groups will decline.

I shall make a special plea for another rare type of individual - the physician/scientist; those who by training and bent, focus on basic biological problems related to human physiology and disease. Their double-barreled expertise is especially needed if we are to successfully apply the powerful methodologies developed during the past few years for understanding the molecular and genetic basis of disease. Presently, the Medical Scientist Training Program meets some of that need but it too is in jeopardy of being eliminated along with other training programs. If anything, this program should be expanded so as to facilitate the transfer of knowledge and techniques from the bench to the bedside.

The achievements made during the last fifteen years have already vindicated the judgment to support untargeted research in molecular biology, genetics, cell biology and biochemistry. From it an extremely powerful paradigm has emerged for analyzing the mechanisms of disease at a level no one would have thought possible in our lifetime. This brings us to a new frontier, one which permits a more rational approach to the prevention and treatment of disease.

The following list of crippling or lethal diseases can now be analyzed at the molecular and genetic level and, as a consequence, our efforts for their prevention and cure can proceed on a solid footing rather than by guesswork.

1) LDL receptor deficiency

2) Cancer

3) Diseases of the immune system

4) Endocrine disorders

5) AIDS

6) Mental illness

At Stanford, we are presently developing a Center for Molecular and Genetic Medicine. Its purpose is to expand our abilities and efforts to advance the basic science in a milieu of physician/scientists. Their aim is to explore the potential of the new breakthroughs in basic science in various areas of medicine. Similar developments are proceeding at several of our research institutions - but in each case their establishment and success will depend upon government policies for support for construction, renovation, equipment and talent.

Does industrial support provide an alternative or supplement to Federal programs? I'm afraid not, although there are some interesting attempts for them to help. First of all, the corporate culture is geared to short term results and proprietary ownership. Both are the antithesis for the kind of stable support that projects with no immediate applicability or payoff require. For example, how forthcoming was industry in the 1950's and 60's when much of the groundwork for the biological revolution was laid? Since it was not easily forseeable how research on bacteriophage and E. coli and its enzymes could possibly pay off industry shunned interest in or support for such investigations. And yet, in retrospect, that's where the ideas, methods and people that created our biotechnology industry emerged from. Can we expect them to be any wiser in identifying the sources of the next biological revolution? Will the breakthrough come from developmental biology, neurobiology or some as yet unexplored and unfashionable field? Personally, I have yet to see the evidence that industry is prepared to, or would consider, investing heavily in the university research enterprise particularly if the information that is to be gleaned is to be available to its competitors as well as to themselves.

I do not believe it is reasonable for this Nation to rely wholly on industry to support basic research. That sector can provide special kinds of assistance but it is unrealistic to expect that the basic biomedical science enterprise could flourish or even survive from that sponsorship alone. Here too, the Packard committee proposed that industry be granted tax credits commensurate with their support of university research programs, servicing equipment and of merit-based scholarship programs. Perhaps, that incentive could have an impact.

Mr. Chairman, I have given you my frank views and I'm prepared to answer questions or respond to your comments.

DISCUSSION

Mr. **Walgren**. Well, thank you very much, we appreciate that. There is this great current in the argument these days about the importance of the peer review system and the importance of scientists making all the decisions as to allocation. How do you look at that, looking back on the development of our capital structure? And by that I mean, I am thinking when during the sixties, there was building going on almost everywhere that I remember on university campuses. I know the buildings at Stanford, and I know some at the institutions that I went to, and some in my own hometown. How completely were those investments driven by peer reviewed quality allocations?

Dr. **Berg**. Although I don't know the cases you referred to in detail, my understanding is that peer review played a major role in the decisions to proceed with the capital investments. I don't for a moment doubt that political and geographic considerations were interjected, but I don't know to what extent they affected the decisions. I believe that the best institutions were supported because they had the talent, ideas, and lacked the resources, so they sought the Government's help.

Mr. **Walgren**. How do you view what is going on in Texas where, as I understand it, they, at least for a while there, were assembling large amounts of money and State-level initiative essentially to create in a place—where there was certainly a base for it, but they were drawing into a site really because of their loyalty to a geography—quality scientists and making heavy investments in what will be, I am sure, the finest scientific enterprise that we have. And yet to the degree that it was geography determined, that would seem to run contrary to the proper investment of that money.

Dr. **Berg**. Well, I think you are referring to the Bobby Inman-catalyzed development of an electronics center. Judging the success of it is a bit premature. We have to wait and see how that turns out. I'm certain that geography plays a role. I think the University of Texas is an asset that probably was attractive. There was certainly an attempt by Mr. Inman to ensure that the educational facilities that would be available to people who participated in that venture were of the highest quality. I think there were a lot of promises made. We have yet to see whether those promises will have paid off.

I think just to look back on the developments around Stanford, there is no question but that the presence of Stanford, and not just the sunshine, was a major driving force in causing the electronics industry to flourish in that area. The interplay between the two cannot be diminished, there is no question about that. But in large part, Stanford's role in that was fueled by Federal funds.

Mr. **Walgren**. To the degree that an industry plays a matching role and is necessary for some local match of the money, and let's say an industry like whatever Mr. Packard's industry is——

Dr. **Berg**. Hewlett-Packard.

Mr. **Walgren** [continuing]. Obviously they have a great personal stake in Stanford and in the bay area.

Dr. **Berg**. Yes.

Mr. **Walgren**. I am sure they would be willing to provide substantial industry contributions and matches for projects that would be proposed in that area, yet their interest has a geographic base to it.

I guess what I am trying to get at is that on the one hand we have the scientists coming and saying let us make these decisions in a totally quality-based review system, and no other kinds of considerations have any legitimacy. And in fact, I think you say that in your testimony: "political, geographic or other irrelevant criteria." Yet our system, in reaching for these industry matches, certainly emphasizes the geographic loyalty of an industrial base, does it not? Would that undercut the most effective allocation of these monies?

Dr. **Berg**. Yes, sir. What I intended by that statement was I believe that political considerations have often overridden peer judgments of quality to assure appropriate geographic distributions. I believe such considerations are appropriate. That is not to say that the east and west coasts should be the only two places where high quality science going on; not at all. It should be every place where it exists, or the promise of it is clear. But, facilities ought not to be provided because of the political influence or some back-room deals. In the last few years there have been several institutions which have received Federal funding by a mechanism that bypassed completely the peer review process.

Mr. **Walgren**. To the degree that our investments in science have been based on military investment that the Government makes, and in your testimony you emphasize how almost completely that is, a real peer reviewed determination has been relatively diminished, has it not?

Dr. **Berg**. Yes.

Mr. **Walgren**. And in fact, I guess you would say to the degree that the U.S. investment in science has been driven by the military allocations, peer review has not played a dominant role at this point?

Dr. **Berg**. For sure.

Mr. **Walgren**. Apparently there are some measures of merit that have been brought to bear, but by and large, those allocations were made by a relatively narrow bureaucracy and a relatively autocratic bureaucracy in terms of the power of the individual decisionmaker.

Dr. **Berg**. Yes, I think so. I was astonished at the allocation of research funding by the military cited in the Packard report. Moreover, in terms of strengthening the basic research capability in this country, that $100 billion does very little. Some, but not as much as it could.

Mr. **Walgren**. One view would be looking back at our system. It is not that we have had the dominance of peer review in the allocation of capital costs, at least from the Federal Government, to the degree that it is occupied by the military investment—and that that is now being changed and threatened—but in fact, looking back, we probably have not emphasized peer review enough in the whole history of our investment in science, and should be doubling our efforts.

Dr. **Berg**. I think at some levels it was the ruling paradigm. At the National Institutes of Health, study sections composed of practicing scientists provide the peer reviews process, and no grant is awarded without such an examination.

Mr. **Walgren**. The National Institutes of Health kind of stands out?

Dr. **Berg**. NSF has relied on very much the same procedure in the field of biology. In the areas of construction, I am a little less familiar with it. But in fact, I am less familiar with it because so little of it has been going on the last 10 or 15 years that we haven't had any practice, and we have let the whole thing drop.

If I can make one point, it is I think we have to find a way for the Federal Government to be able to support the enterprise which it wants to have in place, and to fuel it with the funds to build the facilities. I find it extraordinary that the Government says, "We are willing to give you the money for the research, but we can't give you any of the money for the space to do it in." This is true for a number of foundations as well. They have in their guidelines very generous criteria for awarding funds for research, but they explicitly say they will not support the capital. When you confront them saying, "Where are we going to do this? How are we to break into a new area? How can we expand our involvement in those promising things?" Well, they have no money for that. It has been very difficult, I can tell you, to develop this Center for Molecular and Genetic Medicine—a $50 odd some million building project. It has not been an easy chore trying to raise money from the private sector.

Mr. **Walgren**. Thinking of biological medicine compared to other sciences, or biological science compared to other sciences, the NSF and National Institutes of Health—NSF playing a relatively small role in a large sense, of what we are trying to look at—NSF and the National Institutes of Health have really emphasized peer review.

Dr. **Berg**. Yes, sir.

Mr. **Walgren**. Much of the other Federal investment has had a more limited emphasis on a true peer review system and merit selection in their investments. Perhaps it is not by accident that biomedical science has provided some of the best breakthroughs, and, by comparison, it may be that other areas of science that have not been as concentrated in a peer review sense, perhaps have progressed less rapidly.

Dr. **Berg**. Well, if I may make one point. A peer review system provides a diversity of inputs. Oftentimes, projects that look like they might be going nowhere; they are so far removed from the objective of what the finding agency is, and might not ordinarily be funded. But because there are people there who recognize the importance, the opportunity there, it will be supported.

If you have a group which has no such peer review, but has a mission, and looks only to fund only research that supports its mission, it is a very narrow view. Who knows where the discovery is that is going to best support that mission? The peer review system has allowed a broader base of investigation and therefore discovery, and so the next generation of breakthroughs. I don't think there is anybody in this room, or anywhere, who knows where it is going to come from. The best thing we can do is fund the best people doing the best research as judged by the best people in the fields.

Mr. WALGREN. Mr. Brown.

Mr. Packard.

Mr. PACKARD. You are very kind, Mr. Brown.

Thank you, Mr. Chairman.

Your comments I thought were rather succinct and rather timely and interesting in regard to the replenishing of new, excited, young scientists coming out of our schools. What do you think excites young people in the high schools or junior high schools, early college training level? What excites them in terms of the sciences? Is it a major project, an exciting project, like putting a man on the moon. When those major goals that are set, does that tend to do it? Is it the love of basic research, does that excite young people? What do you think really does attract young, bright minds into the scientific world?

Dr. BERG. An exciting challenge.

Mr. PACKARD. What kind of challenge are you talking about?

Dr. BERG. To find something new, something the world has never known before. To solve problems. There are probably as many different reasons why people do science as there are people. But I suspect that the excitement of being at the very boundary of our ignorance and trying to find out some new things is what excites most people who become scientists. You can't do that if you are starving, and you can't do that if you are pumping gas 6 hours a day in order to support yourself to be able to do this science.

Mr. PACKARD. I think that we are hearing over and over again in these hearings the need to strengthen basic research. And it appears to me there is a little bit of a tug for those funds for basic research, but at the same time, a recognition that basic research does not attract young scientists, particularly at the early ages, so that they do the basic groundwork in preparation to go into a scientific field. That needs to start back at the junior high and high school level, I presume, at least to some extent where they being to become attracted and certainly excited about it.

Do you think a special big project tends to have an exciting aura about it?

Dr. BERG. I suspect they highlight, but I don't think they are a major motivating force. They may persuade some people to go. This is my own view, just my own experience. I went on to graduate school because, when I worked in industry during the summers, I saw that the people who had Ph.D.'s were telling everybody else what to do. I decided that is what I wanted to do.

When I went to graduate school, I discovered a whole new world, a new way of living, and a new way of thinking about the world. The discovery was not based on making a product that was going to make the company I was working for wealthy or prosperous. What excited me was the challenge of finding out something new, of being caught up in a problem, where there was tremendous excitement and respect for the integrity of the people that I came in contact with.

The period of the molecular biology revolution, if you call it that, during the fifties and sixties, was one such period. It was not trumpeted in the newspapers. It was not a national goal. Solving the genetic code came without any formal declarations. That was our target. Nor did the breakthrough come from setting any target. It came when somebody, a few people, saw that the tools and tricks of the trade enabled us to do something different, and that opened up a whole new world. And that is the way science progresses, a few people—sometimes it is luck, sometimes it is just being in the right place—a few people, but primarily students, being together, working together, actively exciting each other, is the way progress is made.

I think if you look at that list of diseases, I could give you a whole lecture on how the progress in the last 5 years in each of those area has totally changed our conception and the possibilities of how to deal with those diseases in the future. That is why we are trying to develop this center at Stanford. It is to begin to move that into clinics and bedsides as quickly as possible with people who understand the language, have been trained in that area, but also have the problem of dealing with sick people.

Mr. PACKARD. It appears to me that money tends to drive a great deal of this whole issue of how not only to attract young people into the scientific world, but it also drives what kind of science goes on. It gets into other questions I will have in a moment.

You mentioned in your testimony that there are not nearly enough physicians, for example, going into research, into science rather than into practice. I have thought a lot about that also. Again, money tends to drive that decision often. It is considerably more lucrative for them often to go into the standard practice of medicine rather than remain in the universities and doing research. What could be done to change that?

Dr. BERG. There is a remarkable program that the Federal Government supports, this Medical Scientist Training Program, which as I say, is in danger of being phased out. It is an attempt to telescope the research, and the medical training, so they are done almost simultaneously. The period of training is some 7 or 8 years, during which they do intensive research as well as learn to be physicians. What it does, it gives them the opportunity at that point to decide what track to follow—and it isn't money I think that drives them, it is opportunity. If there is an opportunity to be able to practice what you have learned, to do research in a medical setting, and to not starve doing it, many people will do that over going out into general practice.

What we have found is that many of the people trained in this way are forced to go into clinical practice because there is no alternative, there is no place for them to work. There is no funding for them and the less the funding, the more patients they have to see. And the more patients they have to see, the less they are aware of what is happening in the world, and the rate of obsolescence in this field is so great, that physicians who graduated 7 or 8 years ago, are illiterate with respect to the language we are talking about—the molecular basis of disease.

Mr. PACKARD. If more funds are transferred from your defense-oriented types of research, space programs, equipment, and laser satellite technology, multitudes of technology that isn't earmarked—I think you indicated about 92 or 93 percent is going to military types of research—if there was a transfer more to basics from military, would that augment your concern, or would it more satisfy your concern about young people coming into the field?

Dr. **Berg**. It would depend on who was giving it and what strings were attached. If the funds were transferred into the National Institutes of Health or the NSF, I would applaud, because I think then it would be used in ways in which we have been discussing until now. If it is the military giving the funds for doing the basic research, I would have to see what kind of parameters it sets before I would say that I think that that would be sufficient.

Just to give you one example, if, in fact, part of the military budget were applied to biomedical research and it helped a cure for AIDS, it would have an impact on the military as much as on the civilian population. You are not going to find the kind of basic research funded by the military that is going to lead to that kind of cure.

Mr. **Packard**. What this committee is trying to do or get is the information necessary to develop a national science policy that will balance out the limited funding resources that we have. At the same time, that balancing act will solve some of these ancillary problems that relate to, as you have related in terms of capturing more bright young minds into the scientific world, keeping more physicians in research areas, rather than into more remunerative areas, and a multitude of others. That is the thrust of my question.

One last question, Mr. Chairman, if I may.

You mentioned the need for more moneys to be earmarked for capital improvement for the facilities, buildings, to do the research in and maybe other equipment to do research. I think that is understandable and of concern to us, too. I guess the question is, should we divide—again with limited funding—should we take more of research-targeted moneys to build buildings, recognizing that that would mean less money for research? Do you think that most of our research institutions would recommend that, that they would like to see, if the question was put to them—if there is $100 million—do you want more of that $100 million earmarked and targeted for building, therefore, subtracting from the research end, or should the Federal dollars be more targeted as present policy would dictate, toward research projects and research money and leave the buildings to schools and universities, to the private sector, et cetera?

Dr. **Berg**. I don't have any magic formula and I would say it is not either/or. I think it is to be both, but let me say——

Mr. **Packard**. Your answer would be we want more money?

Dr. **Berg**. No, no; let me point out a very key point of the Packard Committee's proposal; there was the word matching funds. I was very struck by, at least, what seemed to me if not necessarily innovative, at least encouraging: it is that if we are going to, in fact, interject or inject new funding, it ought to be on a matching basis. I think that is a very clever way of expanding the capability, or using the Government to catalyze that kind of opportunity and allowing the private sector to match it. So, that would be one.

The other, which I was talking about is tax credits—toward industry, for support of capital construction, equipment development, and support of students—as another device of expanding the pool of funds without it necessarily coming only from the Federal Government.

Mr. **Packard**. Thank you.

Mr. **Walgren**. Mr. Brown.

Mr. **Brown**. Dr. Berg, I consider the contribution that you make to be invaluable to the education of Congress. I think one of our fundamental national problems is that in every area, not just science, we have failed to concentrate on the processes which produce quality and excellence. That is true in our industry, as well as our sciences. If we had a good peer review system for making industrial decisions with regard to improving our competitiveness we would probably be a lot better off.

This idea of young people, and I hope old people, being attracted by the excitment of generating new knowledge, of solving problems, is one that is intrinsically very powerful. I want you to understand that I agree with you on these things.

On the other hand, I think you underestimate the importance of the ideas that the chairman and Mr. Packard brought up about the drive for geographic distribution of science funds and things of that sort. I am reminded that in the days when your institution was founded by a great genius of industry, it was a hick college, and the centers of excellence were all back East in Harvard and Yale and some of the other places, and he could easily have been accused of pursuing a fruitless geographical distribution of resources for ego, or whatever reasons.

The fact is the excellent minds go to where there are excellent resources, and there is no valid reason why you shouldn't put those resources where people are, because there is no evidence that the distribution of the finest minds is concentrated around Stanford or Harvard or anyplace else. That is why Texas is moving so vigorously to bring some of those fine minds to centers of excellence there, which is laudable.

And you may have noted that there is a large concentration, undue concentration of Nobel Laureates emanating from Switzerland. There is no real reason for that except CERN is there. Somebody decided that they needed geographical distribution in large-scale high-energy physics machines, and they put it at CERN, and a lot of good people go there to their work, and it gets them a Nobel Prize. And that is the motivation; it is not the grasping, greedy idea we ought to have equal distribution of knowledge, it is an endeavor to create excellence where it doesn't exist. The same thing that led to the creation of Stanford actually. Can you appreciate that?

Dr. **Berg**. Well, I think I take issue with it because I wasn't there at the birth of Stanford, and I wasn't there at the time after the War when it began to emerge from obscurity, although I hope my Stanford colleagues will not take that word obscurity too literally. In any case, I think it was a vision of a few people, and I think a few key appointments, major decisions about people, is what brought and changed the situation. It wasn't anybody saying: "We need to enrich the Bay area, and create an institution that will then allow American industry to gravitate to there and form the electronics thing." It was a few people. And they, in turn, helped recruit additional people, and the thing grew expeditiously because of the people, not because of the decisions that we ought to have something south of San Francisco that we can point to with pride. So, I believe it was people-driven, and not an attempt to equalize the geography.

Mr. **Brown**. We have a problem with geographical distribution of physicians. There is no real indication that health care problems tend to exist mostly in San Francisco and Beverly Hills, but the physicians gravitate there. Are they looking for centers of excellence or what?

Dr. **Berg**. Well, I think it is complicated, it is not quite as trivial as I think you have just said. There are some of these physicians that go to places where they have access to excellent facilities, not just wealthy patients. Being close to a center, such as in the Boston area, and the Boston community hospitals, is a place where a bright young physician might want to be because that is where the action is.

Mr. **Brown**. We spent more money on biomedical research in the health sciences than any other country on earth, and yet we rank about tenth in terms of the health standards of our people. Do you have a good reason for that?

Dr. **Berg**. I bet we rank number one in the area of discovery and development of new knowledge in the biosciences.

Mr. **Brown**. We do, no question about it. The reason for that is to improve the health.

Dr. **Berg**. My problem—my responsibility and problem—is the discovery of new knowledge, and the translation into practice where it affects the health of the public is not where I have been involved. I hope to become involved in that, at least in my local environment, but I think that it is a big problem. That is a problem you gentlemen have had to face more than I have.

Mr. **Brown**. I am trying to give you an insight to our problems.

Dr. **Berg**. I understand that.

Mr. **Brown**. Because I appreciate the contributions that you have made really. I hope you will appreciate that.

Thank you, Mr. Chairman.

Mr. **Walgren**. Thank you.

Well, on behalf of the committee, we do appreciate your coming and being a resource to us, and we look forward to batting things around with you perhaps in a followup.

Dr. **Berg**. Thank you.

Mr. **Walgren**. Our next witness is Dr. Young, I believe, Commissioner of the Food and Drug Administration.

Welcome to our session and please proceed and outline and underscore what you would like to focus on. Then we can have time for discussion.

STATEMENT OF DR. FRANK E. YOUNG, COMMISSIONER, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ROCKVILLE, MD

Dr. **Young**. I will not read any of my statement but instead, I would like to provide a perspective of the research as I know it based on a quarter of a century of activities in research prior to joining the Government.

Dr. Berg and I have the privilege of being trained in the same institution in Cleveland, Ohio, a few years apart, and as he has chosen more to move into the development of a new field in Stanford, I have had the great privilege of moving to the Federal Government as a public servant, because of the very great interest that I have in the very topic that you are describing at this hearing.

We both, Dr. Berg and myself, are products of the National Institutes of Health training grant system; I went into science and finished my M.D. degree and my residency, intrigued because of the opportunities, at that time, of combining both a career in research and the practice of medicine.

The focus on research that I will be providing for you is not that of basic research, of which I was a devotee for an excess of a quarter of a century, but instead, as it applied in an organization that has a responsibility of acting either as the facilitator or the barrier to bringing the fruits of science to society. It is in a sense, Mr. Brown, the area that you were addressing earlier on how basic science is applied.

Mr. BROWN. I can take either side of the issue.

Dr. YOUNG. I am sure, and look forward to discussing both sides with you.

The focus that I would like to provide first is that of the Public Health Service. You have been giving much attention to the National Institutes of Health, which is a citadel of biomedical science, and which has the responsibility in its mission for not only funding research, basic research within the Nation, but of training the young minds and the young people coming forward. There is no more critical area, I would submit for the record, than the role modeling and the bringing forth of the brightest and best, not only in science, and not only into medicine, but, I would submit into the Government as well.

This cultivation of these minds is a responsibility, just as surely as is the biological imperative of reproduction, which brings us the next generation. The Centers for Disease Control focuses on the epidemiology and the analysis of disease patterns that enable us to unravel such complicated diseases as AIDS or other crises and significant problems facing the Nation.

The Alcohol, Drug Abuse, and Mental Health Administration draws its attention more to mental diseases and research in neurobiology; the Health Resources and Services Administration focuses in large number on health systems and health systems research and unique areas of interest, such as Indian Health Service. But it is FDA's role to combine and utilize the science that is developed elsewhere in the Government and in university sectors, and, coupled with its own scientific base, to bring new technology to the American scene.

Why, therefore, must an agency that is primarily regulatory, focus such incredible effort on its research base and its scientific base? First, I would submit that the most critical issue facing a regulatory agency, such as FDA, is that its decisions and actions must be based on sound science. In the absence of that, we would be buffeted and the American people would be poorly served.

For example, in the recent Tylenol tampering crisis that we just went through, it was the ability of FDA, based on years of research in analytical methods, that enabled us, within minutes to hours, to identify by "fingerprint" the type of cyanide that was within those capsules and to determine epidemiologically by traces of metal contaminants whether that cyanide was similar to the one in Chicago, similar to the cyanide used for the suicide in Tennessee, or in fact was different.

We were able within 72 hours, by using these methods, to determine that the case in Tennessee was not terrorism but was in fact suicide. Years of analytical methodology were required to have this capability immediately available for national needs.

Similarly, to screen within a few days over 1.5 million capsules by various scientific techniques required a scientific base (see app. 3). These are some of our emergency functions.

In another realm, the scientific base is required for sound regulation. Aflatoxins, a naturally occurring carcinogen present in peanuts and grain due to the growth of fungi, can produce a problem for mankind. How much is a risk, how great, how to establish acceptable levels? The whole field of risk assessment is based on science within FDA.

The development of regulations in regard to hypersensitivity to sulfites within the population again falls into that category.

The compliance activities that we must undertake enables us again to use sound science to match risk and risk management. Probably the most critical area for science for us is in the new approval process for new products.

FDA can either stimulate or retard the advance of technology. For example, the drug approval process takes 25 months. With the appropriate increment of our scientific base, our reviewing base, that can be dropped readily to 12 months. One can look at such critical medicinal compounds, about which biotechnology is a part, such as the human growth hormone just approved last year. Previous to that approval, we had to use pituitary glands from cadavers, in some cases contaminated with a slow virus. Now we have approved a biotechnology product that makes a big difference. If that had been approved a year later, there would be other individuals that may have unduly suffered.

All the medicinal compounds that come on the market, all of the medical devices, as simple as a thermometer to as complicated as an artificial heart, all of the animal drugs, the whole array of compounds used in the cosmetic industry and the food industry, must be approved by FDA. Thus, 25 cents on each dollar that you and I spend are for products evaluated for safety and effectiveness by the FDA.

Without a sound scientific base, we could not make these decisions or would make them more slowly. In the absence of data, our best defense is to move slowly and you know at times, FDA has used that defense. Therefore, we are served best by a strong cadre of intramural scientists, because our research is different than that of the National Institutes of Health which focuses primarily on applying science to national needs.

We have used mostly intramural research. These research programs by and large are peer reviewed, and are designed to meet our mission in public health. They are not overlapping in any substantial way, to my professional knowledge, with those done in other sectors of the Government. The programs are not, as Dr. Berg would clearly say, the type of research to which one assigns Ph.D. student, or a postdoctoral fellow, or a faculty person.

The total grants in FDA constitutes less than 2 percent of our budget, but there is one program that I would call your attention to that is extraordinarily important, and again, not duplicated. We have a program for orphan diseases. Many of the diseases cited by Dr. Berg would fall into the category of orphan diseases. Under this program, peer reviewed grants are given to both industry and academia and others within the private sector, to study and develop medicinal compounds, and in some instances devices, that could be developed where the economic system would heretofore not support such investment in the private sector. Last year alone, 10 orphan products were approved by the FDA.

The final area that I would focus on is that of a national emergency. In the case of AIDS, FDA was able to approve the test for the AIDS virus antibody in 11 weeks, primarily because we have what we call scientist/reviewers. It is these individuals who were involved in the review and who were also doing research on the very same areas of biology, and so they could, with their own first hand knowledge, in a rapidly exploding field, apply that knowledge to the approval of this product.

I would submit, sir, in the absence of such a strong scientific base, FDA would be a bit ineffective in its capacity to best serve the American public, which I, like you, are pledged to do.

[The prepared statement of Dr. Young follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT BY

FRANK E. YOUNG, M.D., Ph.D

COMMISSIONER

FOOD AND DRUG ADMINISTRATION

PUBLIC HEALTH SERVICE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SCIENCE POLICY TASK FORCE

COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

APRIL 24, 1986

RELEASE ONLY UPON DELIVERY

Mr. Chairman:

I am pleased to have this opportunity today to participate in your review of Government policies for the support of biomedical research. I believe that this is a vital and appropriate subject for Congressional study during a time when emerging new technologies are revolutionizing the way pharmaceuticals are made and offering the prospect of dramatic and hitherto unimagined new products and medical treatments. Indeed, much of my medical background is in biomedical research and I am honored to say that the expert witnesses testifying during these hearings are my colleagues and friends.

RESEARCH AT FDA SUPPORTS AGENCY MISSION

I would like to discuss with you this morning the kinds of research we conduct at the Food and Drug Administration (FDA) and to explain how that research supports our ability to carry out our regulatory mission. Under the Federal Food, Drug, and Cosmetic (FDC) Act and related laws, the FDA is responsible for ensuring that the Nation's pharmaceutical, biological, medical device and radiological products are safe and effective and that the food supply is safe and nutritious.

In discharging these responsibilities, we oversee over 95,000 establishments producing several hundred thousand products, including complicated devices such as the artificial heart. These products, which account for 25 cents of every consumer dollar spent, include all medical devices, as well as human drugs and vaccines and animal drugs, thus influencing over 65 percent of the practice of medicine. Our decisions must be based on state-of-the-art science; thus research is an essential part of our mission. Without highly qualified and trained biomedical scientists and physicians, we could not fulfill our responsibilities.

FDA reviews new products before they enter the marketplace, inspects manufacturing facilities and takes corrective action to remove products from commerce when they are unsafe, ineffective or otherwise adulterated or improperly labeled. To accomplish these activities, FDA must maintain an up-to-date expertise in many diverse scientific areas, including biology, chemistry, microbiology, pharmacology, toxicology, biostatistics and clinical medicine. A significant part of this expertise must serve to provide the Agency with a strong institutional research capacity that can quickly fulfill needs that are unique to the FDA regulatory mission.

Public Health Emergencies (e.g., Tylenol and AIDS Antibody Test)

FDA's research, for example, must be able to develop quick, accurate, sensitive and reproducible methods which can be applied in response to public health emergencies. In this respect, FDA's research is different from that funded by the National Institutes of Health, whose research is of universal interest and which, for the most part, is being conducted worldwide by other medical institutions as well. Without FDA's own in-house research program, the information needed--sometimes quite urgently--by the Agency simply would not exist.

The recent, tragic tampering of Tylenol with potassium cyanide, for example, required a close examination of the poison to determine whether it was added to the Tylenol at the manufacturing facility or at the retail level. To accomplish this analysis, FDA scientists developed what forensic specialists call a "fingerprint" of the particular batch of cyanide found in the Tylenol capsules. This "fingerprint" consists of the total elemental composition of the poison (i.e., the cyanide with contaminants unique to the batch) which is determined through a special type of spectrometry known as an inductively coupled argon plasma - atomic emission spectrometric procedure. The technique can measure precisely traces of chemicl elements at concentrations of parts per billion. Thus, every batch of potassium and sodium cyanide produces a unique spectrum due to its particular contaminants and can be traced back to its point of manufacture. To date, more than 600 spectra of potassium cyanide compiled in FDA's reference library will facilitate identifying the manufacturing origin of this poison should the need arise again. During the recent Tylenol crisis, our scientists "fingerprinted" the cyanide while others used recently developed methods to rapidly screen capsules for cyanide. This is an example of Science Applied To National Interests.

A second example illustrates how FDA research findings must often be rapidly translated into the development and approval of products critical to the public health. In this regard, research by scientists in FDA's Center for Drugs and Biologics (CDB) resulted in the licensure of the HTLV-III antibody test less than one year after the discovery of the AIDS virus. Specifically, our previous research on the transmission of the hepatitis B virus and our research program to develop better tests to screen blood for hepatitis B, provided a framework. Because both the HTLV-III and hepatitis B virus are transmissible by blood and blood products, this basic research done by FDA scientists on hepatitis was of enormous value in understanding the mechanism of transmission of AIDS. FDA scientists with this experience worked with manufacturers to rapidly evaluate a screening test for HTLV-III antibodies in blood. In addition, our hepatitis research efforts to develop heat and chemical treatments to inactivate the virus in products made from blood, which are essential for the treatment of hemophilia, enabled us to apply this same expertise to the development of new procedures to inactivate HTLV-III in an effort to improve the safety of these life-saving products.

Long-Term Responsibilities (e.g., Aflatoxins and Risk Assessment)

Other FDA research enables us to meet more long-term regulatory responsibilities. Two examples that come readily to mind involve our aflatoxin studies conducted by scientists in FDA's Center for Veterinary Medicine (CVM) and our risk assessment research being conducted at the National Center for Toxicological Research (NCTR) in Arkansas.

Aflatoxins are dangerous chemical by-products of molds that can contaminate food commodities such as corn and peanuts and, to a lesser extent, wheat and rice. Although data became available in the 1960's and 1970's about levels of aflatoxins that could be consumed by meat-producing animals without hurting the animal or posing a risk to humans, little was known about the relationship between aflatoxins in feeds and residues in cow's milk. CVM scientists conducted extensive research to learn the relationship. We now know that the current permitted level of aflatoxins in feeds is an appropriate level to insure the safety of milk for human consumption. This type of research is not usually undertaken in either universities or industry.

NCTR's risk assessment research is an even longer-term effort with implications that are critical to many important regulatory actions. As I will discuss in detail later in this testimony, our ability to assess the long-term health consequences of exposure to various substances is hampered by significant gaps in information which require the use of assumptions instead of sound scientific facts. We are committed to filling these gaps. A discovery by an NCTR scientist, for example, that microflora in the intestines can activate the toxicity of some agents, has provided us with new insights about the validity of assumptions involving the relationship between amounts of toxic substances that an animal ingests and amounts that appear in tissues. In other words, we now know that certain bacteria that are naturally present in the digestive tract can make substances toxic or at least more toxic than we previously understood them to be. Among other things, this discovery should help us understand how various agents actually become toxic and may eventually contribute to a better understanding of how cancer is caused under seemingly normal conditions. Although not exotic in nature, it is these types of critical questions that FDA scientists must address in order for the Agency to be an effective and intelligent regulator.

Extramural Research (Orphan Products)

As these examples illustrate, most of FDA's research is performed in-house. We do support some additional research through extramural grants. We are especially proud of our grants program for orphan products to foster the development of products for rare diseases and conditions. This program is intended to support the development of products prior to the submission to FDA of an application for marketing approval. In this respect, our orphan products development program already stands on a broad base of NIH-supported knowledge and helps provide a gateway to marketing for products that are critically needed by relatively small populations. So far, we have awarded grants to support the development of 38 products for a like number of rare diseases and conditions. I am submitting a list of these grants for the record.

Research Supports Virtually All FDA Activities

Therefore, virtually all of FDA's activities rely on a base of scientific and technical expertise. Some of the research findings eminate from other governmental sponsored research. FDA not not duplicate these studies. Instead we focus on studies that are closely related to our regulatory mission. I would like to describe for you examples of the research conducted in support of these activities so that you can more fully appreciate how FDA scientists support FDA's mission.

Product Testing and Scientific Review of New Product Applications

The law requires that FDA ensure that the products it regulates and approves for marketing are safe and effective. The responsibility for making these decisions rests with the scientific personnel who review the product applications. These reviewers often are also bench scientists whose research activities enable them to be familiar with the state-of-the-art science and provide them with unique insights upon which to judge the product applications. For example, scientists in CDB who do research on human vaccines also review product applications in that area. Scientists in the Center for Devices and Radiological Health (CDRH) are conducting research to obtain information that will facilitate improvements in the design of prosthetic heart valves that will support the premarket review of both new and existing designs.

Identification of Hazards

To ensure that the food supply is safe and wholesome, FDA scientists must be able to identify contaminants which could pose serious health hazards. Recently, in response to several devastating outbreaks of listeriosis associated with dairy products due to contamination with *Listeria monocytogenes*, scientists in FDA's Center for Food Safety and Applied Nutrition (CFSAN) undertook studies to facilitate the differentiation of pathogenic strains from non-pathogenic *Listeria*. In response to the immediate crisis, CFSAN scientists rapidly developed a selective medium in which small numbers of *Listeria* could be detected among billions of harmless bacteria in dairy products. This method has been adopted by industry and foreign government scientists and has enabled FDA to remove other contaminated dairy products from the market before they caused illness or even death. Rapid diagnosis of microbes is essential to prevent foodborne illness. Thus this field of research is a high priority within FDA. The initiation and completion of this targeted research in a timely fashion was extremely important to protect our public health.

Development of New and/or Improved Physical, Biological, Toxicological or Chemical Tests

In response to the ever increasing number of technological advances in products, FDA scientists must devise or improve tests to ensure the safety of these products. In FDA's CDRH, scientists have developed several approaches to optimize the performance of diagnostic imaging systems so that the patient experiences the least possible radiation dose while the quality of the image is maintained. I am pleased to report that techniques that CDRH scientists helped to develop that describe the overall performance of an x-ray system have been adopted industrywide. These techniques are now being used to investigate the optimization of x-ray systems used in mammography.

Determination and Establishment of Standards and Determination of Product Compliance With Those Standards

Part of FDA's regulatory mission requires the Agency to set standards for the products it regulates. These standards set a level of purity for drug or food products that may contain contaminants or define the performance of certain medical devices. To determine if industry complies with these standards, Agency scientists have to develop analytical or other test methods to make that determination.

As I have already described, research undertaken by scientists in CVM has provided basic information which can be used in the safety evaluation of foods and foodstuffs containing aflatoxin, a natural contaminant that can enter the food chain and ultimately be found in meat, milk and other foods. FDA has a longstanding program to limit dietary exposure to these toxins founded on analytical methods developed by FDA scientists for detecting minute levels of this contaminant that could then be used to support the permissible levels the Agency established.

Research to Clarify Mechanisms Underlying Toxicologic and Pharmacologic Effects

FDA's National Center for Toxicological Research supports the Agency's mission by conducting a variety of research projects on the mechanisms underlying toxicologic effects and the development of risk assessment models for a variety of chemicals. As one example, scientists at NCTR have developed one of the first of a series of biomarkers--or changes in the cell that indicate that the cell might become cancerous--for identifying the carcinogenic action of the chemical compound, arylamine. Identifying markers associated with carcinogenesis provides a measure, at the cellular level, of the biological response of the test animal to the chemical. This information can then be used to estimate the risk to humans of this chemical.

From the above examples it is apparent that FDA research is unique in several ways: it is targeted to support the regulatory mission of the Agency; it is sometimes the only research of its type being undertaken in the country; and it is often needed to provide quick solutions to pressing major public health problems. With that in mind, let me discuss for a few moments where FDA scientific capabilities need to be targeted in the future to continue to provide the sound support for the FDA's regulatory activities.

FUTURE DIRECTIONS

Because the major scientific fields are advancing rapidly, our own research must keep pace with that of academia and industry. FDA's Plan for Action, which we developed during 1984-85 to help prepare the Agency for the challenges of the 21st Century, firmly commits us to maintain a strong intramural science base in those areas necessary to fulfill the Agency's mission and to use science as the major method for decisionmaking. In addressing FDA's most urgent needs for the future, the Action Plan identifies risk assessment, the new technologies associated with biotechnology and microelectronics and nutrition as key targets for additional FDA research while maintaining our current programs described previously.

Risk Assessment

The ability to make assessments of the long-term consequences of exposure of people to substances is critical to many of FDA's important regulatory actions. The Action Plan commits FDA to develop a comprehensive program to evaluate and test, where practical, the assumptions used in risk assessment. The Agency will focus primarily on assessing the risk to humans of compounds contained in the food supply that have been found to cause cancer in laboratory animals.

The methodology for estimating the risk of cancer from substances contained in the food supply employs data from epidemiology, animal tests and other sources such as bacterial tests. Because human epidemiological or human experimental data usually are not generally available in the foods area, animal tests in which laboratory animals are given high doses of compounds are the cornerstone of most FDA risk assessments concerning food compounds. Nonetheless, as I have previously pointed out, state-of-the-art risk assessment contains information gaps that we must currently fill with assumptions.

Examples of some of the important areas in which gaps caused by lack of information must be bridged with assumptions are: (1) quantifying the level of human exposures to agents; (2) evaluating species and tissue differences in the modulation of the effects of chemical agents; (3) estimating the effects of variables such as diet and age; and (4) extrapolating the results of animal data to likely effects on humans. The uncertainty resulting from the use of assumptions in these areas can cause the final result to be uncertain by several orders of magnitude.

Given these sources of uncertainty in assessing risk, it has been believed that the most responsible course available to protect the public health adequately is to use very conservative assumptions. This has been the traditional approach generally used by FDA and other Federal regulatory agencies. This process, however, generates higher estimates of risk than would less conservative assumptions. The traditional approach, in the absence of sound scientific data, leads to Government placing stringent controls over production of and exposure to substances, up to and including a total ban. With more scientific knowledge we may be able to avoid the overly conservative regulatory approach in some instances.

Although FDA's research into the validity of the assumptions used in the risk assessment will be tailored to the regulatory needs of the Agency, we expect this program to be of major interest to other regulatory agencies due to the general use of risk assessment and the commonality of the problems associated with it. Our research should open doors to collaboration and coordination on a broad basis.

New Technologies

One of the greatest challenges facing FDA in preparing for today and for the 21st Century is keeping pace with the ongoing revolution in medical and food technology. The Action Plan commits us to develop specialized internal capabilities in those new technologies most likely to dominate new medical developments and changes with particular emphasis on biotechnology and microelectronics.

Biotechnology, or the application of biological systems and organisms to technical and industrial processes, will undoubtedly generate a host of new products for humans and animals that will require approval by FDA. This technology will pose new challenges for us.

FDA has, in fact, already approved several products of new biotechnology. These include human growth hormone and human insulin made through recombinant DNA, DNA probes for diagnosing certain infectious diseases, and monoclonal antibodies used for diagnostic purposes. In total, approximately 150 biotechnology-developed products have already been approved, most of them diagnostics.

In the future, particular attention will be directed to new human and animal drugs, vaccines, diagnostic reagents, gene therapy, and modified plants for human consumption. Risk assessment, including model microcosm research and stability of gene products and probes, will require extensive coordination of ongoing research and selective expansion of research efforts. Additionally, FDA must focus on the appropriate training for inspectors, specialists for inspection teams, and regulatory consistency within the Agency. Accordingly, a Special Assistant to the Commissioner for Biotechnology will be appointed whose charge will be to review current programs, identify areas for research, coordinate the advisory system for product approval within FDA, facilitate training of field personnel, and recommend to the Commissioner appropriate facilities, equipment and personnel to meet the mission of FDA. The Special Assistant for Biotechnology will also coordinate collaborative extramural programs with universities as required. Additionally, we will utilize the wealth of fundamental research sponsored by NIH to the greatest possible extent.

A second field in which FDA must develop and maintain a strong capacity to support the fulfillment of our regulatory mission involves microelectronics and microprocessors. The field is proliferating out of the laboratory and into hospitals, physicians offices, and even the home. The applications for the technology span a wide range of products, particularly medical devices and radiological products. The challenge for the Agency is to establish a state-of-the-art capability in both human and physical resources for microelectronics and microprocessors to ensure that we can successfully meet its regulatory responsibilities for products that employ this technology and for related manufacturing processes.

One difficulty we face in meeting this challenge is recruiting and retaining young scientists in the area of microelectronics. Indeed, much thought is being given to the problems of recruitment anc retention as it affects the Agency as a whole. The need to recruit and retain young scientists becomes apparent when one realizes that the average age of FDA scientists is now 44. The management portion of the Action Plan thus calls for significant improvements in the areas of career advancement, laboratory research programs and science base. Clearly, our personnel are our single most important resource. FDA's ability to comprehend, review and regulate new products on the cutting edge of technology as well as conduct the research that provides the foundation for our activities requires that we employ excellent scientific personnel. We must maintain an atmosphere in which our scientists can actively contribute to both his or her profession and the regulatory mission of the Agency. He or she must remain current with this particular field through individual research, by interacting with colleagues and superiors within the Agency, and by identifying new problems that need attention.

Recognizing that the Agency is dependent upon the maintenance of a strong scientific program, the Action Plan calls for the undertaking of a number of science-related management initiatives. To attract and maintain scientists, career ladders for scientists will be evaluated with particular attention directed at the adequacy of laboratory resources, recognition of outstanding research, and the establishment of a peer review system for intramural research scientists. Particular emphasis will be directed toward cooperative FDA/university interaction, "mini" leaves of absence for scientific and medical personnel as a function of duration of service and career plans, collaborative research, and interchange between field and headquarters scientists.

Nutrition Initiatives

The Action Plan commits FDA to advance the science of nutrition. As food processing methods and dietary patterns change, the Agency must constantly evaluate and redirect its own programs to provide continued assurance that there is no deterioration in the nutritional adequacy or safety of the food supply.

Although the role of nutrition in health is not fully understood, epidemiologic and laboratory studies have begun to offer important insights that may help people make food choices which enhance their prospects of attaining and maintaining health. For example, people have begun to consume less total fat, saturated fat, and cholesterol, and have curtailed their intake of salt to reduce the risk of high blood pressure. A number of recent surveys indicate that people are more interested in nutrition, are more aware of the actions they can take to maintain health through their daily eating patterns, and are changing their nutritional practices. These changes were accompanied by a general increase in awareness of the American public about the prevention of disease through their responsibility for maintenance of good health. Yet, there is much to be done to improve the health status of Americans through nutrition and to reduce nutritional risk factors in the American diet.

The Agency's work in this area encompasses the entire spectrum of nutrition-related activities. The issues faced by the FDA are at the cutting edge of national nutrition concerns (e.g., infant formula, weight control products, food fortification, and specially formulated foods for the dietary management of some disease conditions). FDA's research efforts are necessarily more applied than basic in nature and are closely related to the Agency's regulatory program. For example, FDA's Center for Food Safety and Applied Nutrition is studying issues such as the nutritional quality of formulated foods and the effects of food processing on the nutritional integrity and safety of foods. Additionally, factors which may affect nutrient bioavailability either positively or negatively, such as processing or particular combinations of ingredients in food, are being evaluated. This work includes a study of nutrients of public health concern, such as the current collaborative studies on iron bioavailability.

In addition, CFSAN is pursuing a nutrition/toxicology program including an evaluation of optimal nutritional needs of laboratory animals to ensure the most accurate toxicology testing programs possible; the determination, in collaboration with other Centers interested in toxicology, of the impact of diet and nutritional status on toxicological end points; and the development of sensitive indications of nutrient toxicity.

The Action Plan also charges CFSAN with developing a comprehensive approach to the analysis of microbial contamination of food using state-of-the-art conventional and biotechnological methods, with particular emphasis on the newly emerging pathogens and microbial problems accompanying technical modifications of food processing.

CONCLUSION

Our research capacity is an essential for the strength of FDA. Our biomedical scientists enable us: to stay abreast of rapid changes in technology and to perfect analytical methods; to develop the appropriate regulations to promote public health; and to be able to react quickly to help solve public health emergencies that can be quite varied in nature. Without this capacity, our decisions would be based on expedient whims rather than solid science.

RESPONSES TO THE COMMITTEE'S QUESTIONS

This portion of the testimony will address the specific questions asked of us in the Committee's letter of invitation to this hearing.

MANAGEMENT OF FEDERAL BIOMEDICAL RESEARCH PROGRAMS

1. What are the agencies' policies for the support of basic and applied research? What strategies are employed for short and long-range planning? What proportion of the budget is used for research? What is the mix of basic laboratory research and clinical research? How much research is performed in-house and in extramural programs at universities, industry, and other laboratories?

In addressing the Committee's concerns about the FDA's support of research, it is critical to understand the Agency's mission and the essential role that scientific research plays in a science based agency. FDA is the regulatory agency responsible for the safety of the Nation's foods, cosmetics, drugs, biologics, medical devices and radiological products. Because of its broad regulatory responsibilities to protect the public health, the Agency activities must be supported by a strong scientific base. Thus, the purpose of FDA research is to generate and gather essential scientific information which the Agency needs as a basis for its regulatory decisions. The development of scientific information by FDA includes, for example, research to identify, reduce and monitor consumer risks and to develop improved methodologies in protocols for the evaluation of the chemicals and other products that come before the FDA for approval.

It is important to understand the distinction between the goals of FDA scientific research and those of other research institutions.

Research undertaken by FDA is often unique and very specialized in that it is aimed at providing information specific to FDA's mission. For example, since Dr. Wiley's time the FDA has pioneered in the development of toxicological test methods. Two-year chronic feeding studies, the technique of in-utero exposure, and skin and eye irritation tests were all first developed substantially through research at FDA. In the area of analytical chemistry FDA is the leader in the development of methods for detecting multiple pesticide residue, and more recently has pioneered the development of analytical methods for aflatoxin and volatile nitrosamines, which are found in foods. For example, research by FDA scientists resulted in the development of quick assay methods for detecting cyanide. This information was used effectively in our latest Tylenol tampering incident. Clearly, although different from the National Institutes of Health's (NIH), the development of these specialized analytical methodologies are essential to protect the public health. Therefore, we build upon the basic research of NIH and apply it to national public health needs.

Because of its unique relationship to regulatory actions, most of FDA's research is carried out in-house, in each of our Centers. The Center for Drugs and Biologics (CDB) has research facilities on the NIH campus. The research program of the Center for Veterinary Medicine (CVM) is located on the Beltsville campus and the reviewing functions are in Rockville. The National Center for Toxicological Research (NCTR) is in a research facility in Little Rock, Arkansas. The Center for Food Safety and Applied Nutrition (CFSAN) has facilities in downtown Washington and a newly developed research building in

Beltsville. The Center for Devices and Radiological Health (CDRH) has both its research and reviewing functions in Rockville.

In addition, FDA supports extramural research through grants and contracts. The extramural program constitutes only about 2 percent of FDA's budget. In contrast to the aforementioned intramural programs, the entire extramural orphan program is a research grant effort. CDB, CFSAN, NCTR, CDRH and CVM use contracts to supplement their in-house research program. Also, several of the centers utilize research support contracts to provide many of the technical services, i.e., animal care, diet preparation, and pathology required to maintain a viable research laboratory.

There are no line items specifically detailing FDA's budget for research. The various research programs and projects are contained in justification for individual programs within FDA's budget. The Agency spends a total of approximately $80 million (salary, support and administrative overhead costs) annually on research, which represents approximately 20 percent of the Agency's total budget. About $10 million of this $80 million research budget is spent on extramural research ($5 million in research grants and $5 million in research contracts).

2. How are the agencies organized for the conduct and support of research? Who sets the priorities and what criteria are used?

3. How are research projects selected? What review mechanisms are used? What are the reporting, administrative, safety, and security requirements? What is the researcher's role in the agency's planning program?

The research planning activities of each of FDA's individual Centers are part of a larger Agency program for annual planning and evaluation called the Program Management System (PMS). Introduced in 1970, this system is utilized to organize the Agency's financial and program information into meaningful and readily identifiable program elements. It is an umbrella system that combines planning, budgeting, reporting and evaluation.

The PMS is composed of a framework based on FDA's regulatory responsibilities in nine program areas, which are further subdivided into 41 projects. A list of PMS projects will be provided for the record.

The PMS structure encompasses all of the Agency's resources, and so provides a common basis for resource allocation and reporting. The PMS programs and projects are not static entities and may change as the priority issues for the Agency change. This program structure is evaluated annually to assure applicability to the Agency's current needs.

Each of the FDA Centers utilizes the PMS structure as a framework for developing a plan for research activities, and each Center independently identifies and ranks its scientific research proposals. Ultimately though, each Center's annual plan must fit into the overall set of priorities and directions set by the Agency in its planning process.

A brief description of each Center's process for research planning follows.

Center for Veterinary Medicine

Intramural Research

The basic function of the Division of Veterinary Medical Research (DVMR) is to conduct studies and develop methodology supporting the Center in both preclearance review and post-clearance surveillance and compliance areas. In addition, certain aspects of the experimental programs are used to support legal action under the Federal Food, Drug, and Cosmetic Act.

Further, the DVMR provides consultation to Center review functions in resolving complex scientific problems requisite to judgments with respect to safety, reliability, and significance of research data.

Cooperative Research

The DVMR also engages in cooperative research studies with other research facilities and programs such as: the U.S. Department of Agriculture (USDA), NCTR, the National Toxicology Program (NTP), and FDA's Office of Regulatory Affairs (ORA) (e.g., Animal Drug Research Center, Denver District office) for the purpose of meeting the individual and/or mutual needs of the participants.

Extramural Research

FDA's limited extramural research programs are initiated to extend the intramural capability in new areas of research for which intramural resources are not available. Memoranda of Need are prepared, reviewed by the CVM Research Committee, and the recommendations regarding the programs are reviewed and approved by the Center Director. In addition to university laboratories, extramural programs may be conducted through contracts, grants or cooperative agreements by NCTR, ORA, USDA, NIH and the Environmental Protection Agency (EPA). Extramural research work is conducted under the guidance of a Project Officer from within the Center and under the supervision of the Office of the Associate Director for Science.

Research projects in the annual five-year research plan are developed by the line managers of DVMR (intramural) and the Office of the Associate Director for Science (extramural). Research scientists are directly involved in determining the intramural studies. Priorities for all research are determined based on current and anticipated needs delineated through continual dialogue with the scientists involved in pre-market approvalof products regulated by CVM. The current demands of the Agency coupled with factors relating to scientific expertise, scientific support and facilities all have an impact on intramural studies. The extramural program is similarly directed to needs of the Agency. Its scope is usually limited by the availability of funds. The five-year plan is reviewed by the Center Director for concurrence and approval.

Center for Devices and Radiological Health

Using the Agency's overall PMS framework, research activities in the Center for Devices and Radiological Health are in four functional areas: (1) bioeffects analysis, testing and method development; (2) monitoring and quality conformance; (3) product evaluation; and (4) training and assistance. To ensure that adequate technical expertise is reflected in the selection and development of activities within these four areas, a system of internal committees has been established. These committees address the different scientific disciplines and subject matter areas under each of the four PMS project areas.

The process of selecting proposals and determining priorities follows:

- A subject matter committee comprised of CDRH personnel technically familiar with the various Center issues, identifies trends, issues or problems associated with the particular disciplinary areas for which the Center has responsibility.
- A set of long-range objectives is developed from the suggestions raised by the committee.
- The long-range objectives are distributed to operating component managers who propose specific activities to meet these objectives.
- Subject matter committee members review the proposed activities for relevance to the long-range objectives, as well as for scientific and technical design.

- The completed operating plan is reviewed by CDRH senior management who make final judgments, resolve priority conflicts and finalize resource allocations.

- During the following year, the subject matter committee provides communication, coordination and informal monitoring of CDRH activities in the prescribed areas.

- At the beginning of each new planning cycle, the objectives and progress in meeting those objectives are reviewed. Objectives may be deleted or changed to meet the Center's and the Agency's needs.

- When a project is near completion, the results are reviewed by both external and internal peer groups as well as other Government agencies, where appropriate.

National Center for Toxicological Research

General policy directives on scientific research for NCTR come directly from the Commissioner. In addition, NCTR utilizes a body of eminent outside scientists called the Science Advisory Board to review scientific directions and to propose future direction. Research planning steps are as follows:

- Individual scientists propose experimental plans consistent with the policy directives for NCTR.

- Experiments may be categorized into one of three types: (1) those requiring less than 250 hours of effort and no resources from other groups within the Center (Type 1); (2) those requiring up to 750 hours of effort (Type 2); and (3) those requiring more than 750 hours effort (Type 3).

-- Type 1 experiments need only obtain approval from the respective division director.

-- Type 2 experiments have to be approved by the Center Director.

-- Type 3 experiments require a more elaborate type of approval:

  - A concise statement of objectives, approach and resources must be approved by the NCTR chain of command, including the Center Director.
  - The approved proposal undergoes the first level of internal peer review (three scientists at NCTR).
  - The second level of peer review by senior scientists comprising the NCTR Scientific Council follows, including an interview with the investigator.
  - After Science Council approval, the proposal is submitted to external reviewers of appropriate, relevant expertise. This is an independent, blind review which is scored the way NIH grants are.
  - High scoring proposals must be given final approval by the Center Director.

- No investigator may have more than two short-term studies underway before starting a Type 3 experiment, nor may scientists devote more than 15 percent of their time to short-term experiments.

Center for Drugs and Biologics

The research programs planned in the CDB largely follow the NIH model with a complex series of interactions taking place between the individual investigators and upper level management. The division director is the key individual responsible for initiating specific research projects. The goals of this research vary widely due to FDA scientists' research findings, and their interactions within the Agency, including CDB's management on up through the Office of the Commissioner. They are strongly influenced by formal and informal interactions with scientists in other Government agencies, especially NIH and the Centers for Disease Control (CDC), academia and industry. A major element which influences the choice of new research projects relates to the types of new products being generated by industry and academia. These projects may be of the "applied" type, for example, the evaluation of test kits to screen HTLV-III (human T-Cell lymphotropic virus) antibodies in human serum. A project may also involve more basic research areas such as research on the biology of viruses and bacteria that are important in product development.

Intramural Research

The particular research planning steps for intramural research in CDB are as follows:

- Research ideas may be generated at any of the levels described above and implementation plans are discussed with the division director as to their scientific merit, feasibility and cost.

- If the project can be performed within existing resources it may proceed. If new resources are required or additional consideration of the program merit is needed, the division director will discuss the proposal for the research with the CDB Deputy Director.

- If a substantial redirection of extensive resources is envisioned the Center Director and the Commissioner's office would also become involved.

- Scientific merit of ongoing projects is reviewed in several ways: These may include discussions in connection with reviews of merit pay and Senior Executive Service plans or project leaders, peer review of manuscripts for publication, and scientific presentations of intramural and extramural meetings. In addition, CDB maintains standing advisory committees which meet several times a year. These committees provide, on a continuing basis, outside peer review for each of the Center's laboratories. The results of the peer reviews are further reviewed by the NIH Scientific Directors and the Deputy Director for Intramural Research at NIH.

- All accomplishments and goals are included in the ahnual report of each CDB division.

- All promotion and tenure actions for scientists are reviewed by the NIH Board of Scientific Directors.
- These reports are used to formulate long-range goals.

Extramural Research

The particular planning steps for extramural research in CDB are as follows:

- A Memorandum of Need (MON) is generated at the investigator level with prior program review and approval by the CDB Scientific Director.
- The MON is reviewed by the Center's extramural science advisory staff to determine technical accuracy, and availability of funds.
- The MON is reviewed by various FDA components with appropriate oversight.
- The research contract, once awarded, is monitored for technical and financial performance by the contracting officer with the assistance of the project officer who initiated the request.

Center for Food Safety and Applied Nutrition

Planning efforts within CFSAN focus around the Center's Technical Plan. The Technical Plan is a computerized, program structured, management information system, instituted in the Center in 1970. It is designed to provide planning data on how total resources within the Center will be used by program, project, and division. The plan relies on program, project, segment and organization managers for developing work plans and projecting research needs. Programs, when taken together, account for the total Center resources. Under this system, the Center has the capability to relate resources to specific problems, account for the expenditure of resources and specify accomplishments.

Intramural Research

Research planning in the Division of Microbiology and the Biological Hazards Program proceeds as follows:

- Each senior investigator drafts a technical plan proposal and submits it to the branch chief.
- Branch chief submits a compilation of proposals to the appropriate division directors or program managers.
- Division directors/program managers evaluate and rank the proposals using several criteria: (1) the urgency of a particular public health hazard; (2) the number of persons/years affected by the hazard; and (3) scientific/technical merit balanced by resource considerations and requirements.

Extramural Research

The extramural research planning in CFSAN is as follows:

- CFSAN's Extramural Review Committee (ERC) meets early in the third quarter of the fiscal year and reviews, evaluates, and ranks all proposals based on scientific and technical merit.
- The ERC is chaired by the CFSAN Director and is composed of Center office directors and the Center Deputy Director. Advising the Committee are the Extramural Science Advisor, the Budget Management Officer, the Executive Officer, and the Director of Division of Program Operations.
- The Center Director determines the final priority of the proposals to be funded based on the recommendation of the ERC.

Office of Regulatory Affairs

ORA encompasses all of the FDA field operations including 20 district laboratories and seven research centers. There are four different programs of scientific research carried out by these field offices: (1) joint planned research between ORA and FDA Centers; (2) research within the Science Advisory Research Associate Program; (3) research at an FDA field research center; and (4) district discretionary research.

All ORA research efforts are coordinated through its Division of Field Science which also facilitates the planning, execution, review and evaluation of ORA research.

A description of the research planning for each type of ORA research follows:

Joint Planned Research Between ORA and the FDA Centers

- Proposals are solicited from headquarters units, district offices, science advisors and field committees (including laboratory directors committees). These proposals should reflect priority areas of research in each district laboratory.

- Research proposals are rated and ranked on scientific and technical merit by the ORA Research Review Committee (which consists of: the laboratory directors, two ORA science advisors, and the Director of the Division of Field Science).

- The highest ranking proposal for each position class (chemist, microbiologist, engineer) are approved depending upon available resources.

Research Within the Science Advisory Research Associate Program

- Proposals are submitted by individual investigators.

- Proposals are reviewed for two requirements: (1) career development for a field analyst/investigator, and (2) full-time research (6 months to one year) on an analytical/investigational problem of major concern to the Agency.

- Approved research is carried out at a local university or college.

4. What is the role of advisory committees in the development and execution of science policy and programs?

The FDA through its various centers uses a variety of mechanisms to provide input and oversight for its research programs. NCTR and CVM have standing advisory committees which meet several times a year to provide outside peer review of NCTR's research contracts and CVM's research policy. FDA's CDB uses several scientific advisory committees in the same fashion as NIH to provide outside technical advice on certain difficult scientific issues associated with particular product applications. The Agency views these types of review as critical to maintaining high standards of research and as a part of its Action Plan, plans to enhance the use of scientific peer review within the Agency.

5. What funding mechanisms are used to provide research funds? Does a certain type of research support result in a greater technological payoff in terms of medical products or improved health care?

The funding for research conducted by FDA is derived through Congressional appropriation for the Agency's overall regulatory and public health mission. In addition, one of FDA's centers, NCTR, receives funds from PHS, EPA, Department of Defense (DOD), and the Consumer Product Safety Commission (CPSC) to conduct collaborative research funded through interagency agreements.

FDA devotes most of its research dollars to intramural research with some allotments for extramural contracts and grants (e.g., the Orphan Product program).

When considering the "technological payoff" of the research FDA conducts, it is important to take into account the Agency's mission.

Though FDA's mission is not to commercialize products, the Agency does control the entry of the products it regulates into the market through its product approval and compliance activities. Insofar as FDA's scientific research supports these regulatory activities, the Agency contributes substantially to the commercialization of new technology.

A good example of this is seen in the area of biotechnology. Because of their expertise in recombinant DNA technologies, scientists in the CDB were able to work closely with Eli Lilly to expedite the review and approval of the first drug product made with biotechnology--human insulin. This same FDA expertise was utilized several years later when human growth hormone made through rDNA techniques was approved. In this case, the "payoff" was even more evident because the human growth hormone made through conventional techniques was found to be contaminated with a slow virus which could endanger the lives of the recipients. The following selected examples illustrate further FDA's role in supporting technology transfer.

FDA's Orphan Products Program are one of the Agency's highest priorities. It is administered by the Office of Orphan Products Development and their efforts in this area have continued to produce results. First, FDA approved 10 new drug applications for orphan products in calendar year 1985. Second, under the provisions of the law, FDA gave orphan designation to 44 drugs in 1985. This designation entitles sponsors of such drugs for rare diseases to tax credits for clinical research expenses as well as eligibility for exclusive marketing approval status, thus facilitating the development of orphan products through the provision of incentive. Third, FDA awarded in 1985 slightly less than $2.5 million in both new grants and continuations for prior projects for studies of orphan products. This includes a one-time transfer of $1 million awarded under an Interagency Agreement with the National Institute for Child Health and Human Development, and permitted the award of 21 orphan product research grants and one contract. This is the largest number of grants awarded since the initiation of the program in 1983. FDA intends to award $2.8 million of FDA's funds for such grants in 1986, and $3 million in 1987, which will even further expand this important effort. Since the inception of the grants program 38 grants have been awarded.

CFSAN's research with CDC has provided new information on factors which effect the bioavailability of lead from various environmental sources including the important interrelationship between lead, vitamin D and calcium. Further, the research showed that lead was retained proportionally higher in growing children then in adults. This research led to the elimination of soldered seams in food containers.

CDRH's research has lead to the utilization of holographic techniques for inspecting hermetic seals for human implant device electronics. This technology is now being applied to detect leaks in drug ampoules and in salmon cans. In addition, NCTR's research in cooperation with the Orphan Products Program has lead to the approval of Trien, an orphan drug for the treatment of Wilson's disease.

6. What are the policies for infrastructure maintenance? What is the availability of adequate, qualified scientific and technical personnel to meet present and projected agency needs?

The FDA like its sister agencies within the Federal structure is concerned about the loss of vital scientific expertise and the subsequent difficulty of replacing them. With the recent introduction of its Plan For Action the FDA has attempted to address the problem of providing an adequate supply of scientific personnel. Proposals in this plan include the Commissioner's advancement program which emphasizes exchange programs within the scientific community, State and local governments and the private sector to aid FDA in keeping pace with advancing technology, and an Agency-wide effort to meet the changing specialized and technical needs of all FDA employees. It emphasizes a cooperative FDA/university interaction through "mini" leaves of absence for scientific and medical personnel, and encourages collaborative research and interchange between universities and the FDA. It recognizes the need for adequate facilities and calls for a master plan for facilities Agency-wide both field and headquarters. As a product of this effort, the Agency will be occupying, this summer, a new laboratory building designed to house over 250 people at Beltsville, Maryland. Architectural and engineering design for a second module at Beltsville is nearing completion. In addition, this fall NCTR will mark the completion of a three-part, four-year construction program that will add substantially to our laboratory capability and support space at the Center in Arkansas. Also, renovation and new construction in Atlanta and Denver Districts will improve the Agency's ability to meet the challenges of both its regulatory and research missions.

7. What are the agencies' roles in the development of scientists and physicians? What training or other programs are available for supporting graduate and postgraduate students and to attract more women and minority students into the national pool of biomedical scientists?

FDA sees its responsibility in developing scientists and physicians from two standpoints: (1) the need to provide an environment and opportunity to maintain an intramural cadre of scientific talent at the cutting edge of technology; and (2) provide a program of continuing education and information for the scientific community at large in order to disseminate FDA scientific policy.

Operating without an extramural training grant program, FDA relies heavily on the NIH programs to provide the pool of new scientific talent. From this, FDA must vigorously recruit post-doctoral scientists for appointments into its staff fellow program and epidemiologist training program. A recently awarded contract to Oak Ridge Associated Universities also will provide the FDA with post-doctoral scientists at NCTR. Once on board, FDA provides numerous opportunities for the scientists to take advantage of continuous education and long-term training. One and two week training opportunities are available in all the scientific disciplines at both private and public institutions across the country. Further, each year the FDA supports 5 to 10 scientists in long-term training positions. As a part of the Action Plan, a cooperative program of FDA/university interaction will provide "mini" leaves of absence for scientific and medical personnel. The annual cost of these programs is one and a half million dollars each year.

Continuing education and information exchange is accomplished through our Office of Health Affairs. We have established and maintained a liaison with a variety of scientific and professional health organizations; including those whose membership consists of primarily minority scientists of health professionals and regularly solicits their assistance in our recruitment. A monthly column prepared by FDA appearing in the Journal of the American Medical Association provides the country's physicians with updates of FDA scientific findings and policies. Several of our Center's have undertaken projects to provide continuing education and training of the country's health professionals. One project culminated in a program to help teach how to read x-ray films that is used widely in the training of physicians and radiologists. We have produced training films for anethesiologists and we developed an anesthesiology procedure checklist to help in detection of common problems.

8. How do the agencies involve universities and medical research centers in multidisciplinary and interdisciplinary research programs? How are incentives provided for joint projects between universities or medical centers, and universities and industry?

In the context of FDA's mission-related research efforts the Agency utilizes outside scientific expertise as both a source of information, as well as, technical assistance. Several of FDA's Centers utilize university staff through formal appointments to Agency advisory committees, working groups, and panels. Even more directly, as reported earlier, several of the Centers through their contracts and grants establish collaborative research projects with universities. At NCTR, for example, an interdisciplinary program in toxicology has been established with the University of Arkansas Medical Sciences Campus. This program leads to a Doctorate in Toxicology, where much, if not most, of the doctoral thesis research is performed on the NCTR facilities. CVM and the Virginia-Maryland Regional College of Veterinary Medicine at Virginia Tech University also have a cooperative agreement whereby research programs of mutual interest to both are developed and undertaken.

9. What are the agency's relationships with the international biomedical science and health communities?

FDA is widely recognized throughout the world as the leader in scientific and technical expertise in the regulation of foods, drugs, biologicals, veterinary drugs, and medical devices. In cooperation with the World Health Organization (WHO), FDA has been instrumental in the planning and organizing of international conferences for drug regulatory authorities, medical device registration authorities, and veterinary drug registration authorities. We have also been instrumental in working with the Food and Agriculture Organization (FAO), WHO, and the Pan American Health Organization (PAHO) in planning and organizing an inter-American conference on food protection for countries of the western hemisphere. These activities and others have led to the FDA being widely sought by other governments as well as international organizations to provide technical advice and assistance as well as technical training in other countries and in the United States.

FDA has had a long and productive relationship with the United Nations health organizations, particularly the WHO, FAO, and PAHO. FDA's Center for Drugs and Biologics serves as a WHO Collaborating Center for the Standardization of Biologics Materials and as a WHO Collaborating Center for International Drug Monitoring. The Center for Devices and Radiological Health has three WHO Collaborating Centers: the Center for Nuclear Medicine, the Center for Standardization and Protection Against Nonionizing Radiation, and the Center for Training Nonionizing Radiation, and the Center for Training and General Tasks in Radiation Medicine. The Center for Food Safety and Applied Nutrition serves as a joint FAO/WHO Collaborating Laboratory on Food Colors and as a FAO/WHO Collaborating Center for Food Contamination Monitoring. At the present time, WHO, PAHO and CDRH are developing an international conference on medical devices to be held this June. In addition, the FDA is extensively involved with commissions, committees, and working groups associated with these United Nations organizations, e.g., the Codex Alimentarius Commission, which establishes international food standards, and the Commission of Narcotic Drugs, which establishes international controls on narcotic and psychotropic drugs.

FDA works closely with other Public Health Service agencies and the Department of State in disseminating and receiving information and coordinating FDA input into international initiatives, e.g., the recent drafting of a U.S. proposal to coordinate the regulation of biotechnology in countries which are members of the Organization for Economic Cooperation and Development (OECD). A recent 24 nation ad hoc OECD working group, through the leadership of the U.S. delegation led by the Commissioner of FDA, was successful in producing a concise and clear draft document that will serve as a significant guidepost for conducting biomedical research that involves the application of biotechnology.

FDA is clearly recognized as the world leader in the dissemination of technical information and in the training of foreign government officials in scientific and regulatory matters pertaining to the regulation of foods, drugs, and medical devices. We routinely provide the expert services of our personnel to participate in international meetings and symposia in areas of biomedical research that directly relate to its regulatory mission. These include expert meetings on biological standardization, specification for pharmaceutical preparations, evaluation of certain food additives and contaminants, radiodiagnostic investigations and devices CDRH is participating in tripartite between the United States, Great Britain and Canada concerning medical device safety and regulatory policy. The project of considerable interest is the development of a uniform approach to safety studies for medical devices.

I am pleased to report that our cooperation and coordination with the international biomedical science and health communities is excellent, and future communications and cooperative activities with these bodies are expected to grow. We have recognized that if we are to continue to meet our domestic responsibilities, it is essential that we maintain and further develop collaboration with our international colleagues who share similar concerns and responsibilities. One way in which we have tried to accommplish this is through FDA's Visiting Scientist Program.

This competitive program allows a small number of foreign scientists to work in FDA's centers for a time ranging from several months to a year. These scientific experts participate in an invaluable exchange of information and technical skills which is mutually beneficial for both FDA and the scientist involved and they build continuing collaboration and information exchange for the future. Furthermore, these programs are essential to improve the quality of FDA regulated products that are imported into the United States.

EVALUATION OF RESEARCH BENEFITS

1. How are short- and long-term goals in biomedical laboratory and clinical research leading to the improvement of public health?

As discussed earlier in the testimony, FDA's research must support both short-term goals associated with the Agency's ability to react quickly to public health emergencies and longer term goals associated with the Agency's ability to ensure the safety and effectiveness of new medical products and the quality of the Nation's food supply. Our ability to "fingerprint" batches of cyanide, for example, enabled us to learn almost immediately whether the cyanide recently found in Tylenol was originating from the same or different sources. Our hepatitis research provided FDA with a base of knowledge that could be transferred rapidly to our review and timely approval of the AIDS antibody test kit. On a longer term basis, our research is focusing on closing the information gaps inherent in our ability to conduct risk assessments of the effects by exposure over time to toxic substances and on limiting exposure to aflatoxins, which are toxic mold by-products that appear naturally in certain foods.

2. What strategies are the most effective in combating disease and in improving health and health care? Is this accomplished best by understanding the disease process? What has been the relative success of therapeutic or preventive strategies?

There are several strategies that are critical to the successful preservation and improvement of the public health. The most important of these is the support for unfettered scientific exploration through basic research. The importance of such research is evident in the rapid development of new biotechnology in the past 10 years. The scientific concepts and techniques which provided the foundation and impetus for this high-tech revolution were developed through basic research in virology, microbiology, and biochemistry. Each of the individual discoveries (e.g., identification of reverse transcriptase, identification and purification of restriction endonucleases and ligase, the elucidation of nucleic acid replication and transcription, etc.) that lead to new biotechnological techniques were the result of basic research on unrelated topics which, in combination, resulted in a new major technology.

Concomitant with unfettered basic research is the support and training of young scientists who can carry out that research. Developing a strong resource of diverse scientific expertise in the United States is essential for the continued development of new and improved technology. From FDA's perspective, the availability of a cadre of young scientists is also necessary to support its regulatory mission (as described earlier in this statement). Because FDA is often the gateway for the commercialization of new products which affect public health, a strong improving health and combatting disease in the following ways: faster approvals of new drug and device applications; more effective post-marketing surveillance of products already on the market, and increased capabilities for assessing the safety and efficacy of products from new technological advances.

Strategies for improving public health must take into account both preventive and therapeutic measures. Clearly, the FDA supports both approaches. In its regulation of new drugs and devices (e.g., implantable defibrillator, lithotripter, etc.) to ensure safety and efficacy, the Agency contributes to the Public Health Services' efforts to combat disease. In the area of prevention, FDA's regulation of foods and food additives and its research and regulation of new vaccines helps to ensure that public health is protected. These regulatory efforts are also coupled with FDA programs to inform and educate both the public and health care professionals about the safe use of products it regulates.

In summary, the most effective strategies for protecting and improving the public health require a partnership between Government, universities, and industry. FDA plays the important role of evaluating new technologies, devising the appropriate regulatory framework, and ensuring that decisions are made on sound science. While neither basic nor applied research alone is sufficient, the combination of sensible regulation based on the risks and parameters defined by good scientific research provides the protective partnership necessary for sustaining and protecting the public health.

3. How are the applications of basic biomedical research evaluated? What criteria are used?

Because of the nature of the Agency's research mission, this question is not directly applicable to FDA. However, FDA's Office of Planning and Evaluation (OPE) has undertaken several studies regarding various aspects of Agency scientists and research. These are discussed below.

FDA's Scientific Innovations

An inventory of their uses by industry, academia, health care providers, and other Government agencies. This report (OPE Study 72, 1985, will be provided for the record) categorizes 56 examples of FDA's participation in developing products and processes that are themselves, or have led to, scientific or technological innovations. FDA's contribution to innovation is not the result of a direct research program, but rather a by-product of the Agency's problem-solving approach to a variety of regulatory issues. The report collects these diffuse and often unrecognized efforts, and examines their use by industry, academia, health care providers and other Government agencies.

Over half of the innovations are in the area of developing instruments and procedures to detect, quantify and reduce known hazards. An example is the "Stoms" meter FDA developed to detect radiation leakage from color television sets. Several other innovations assist in determining the biological effects of chemical and biological agents and of radiation.

Study of FDA Scientists and How They Communicate

The study of FDA scientists and how they communicate was completed by the Office of Planning and Evaluation in response to an interest expressed by FDA management. An Executive Summary of the study will be provided for the record. The decision to proceed with the study was supported by the fact that good science has a central role in the effective functioning of FDA. As a situational analysis, the study concentrated on the present time. Historical information was elicited and used only to a very limited extent.

The study had two objectives:

(1) To acquire a thorough profile of FDA scientists, and

(2) To describe how FDA scientists communicate with others (inside and outside the Agency) concerning technical matters and policy and program matters, and to ascertain the scientists' evaluation of the communication channels.

In addition to age, education and occupational specialty, information was collected from the FDA scientists about how their time was spent among Agency scientific activities. The activities are: critical and systematic evaluation of scientific data for clearance or approval purposes; developing new or improved analytical methods for laboratory application or compliance testing; testing of products or materials to determine conformity with standards; and laboratory studies, epidemiological investigations, and product surveys for the purpose of establishing risk or setting standards. It turned out that the evaluation of scientific data took up about one-third of all FDA scientist time. It was also learned that almost one-half of the FDA scientists were concurrently involved in three or more scientific activities.

The study concluded that FDA had no serious and pervasive scientist communication problems. Nor were there any organization or geographic locations where there were serious localized problems. No management action was necessary.

Technology Forecasting

In 1981, FDA completed its first study to identify technologies which may emerge over the next 5 to 15 years and which may affect or be affected by the Agency. We are now in the middle of the second such study. The first study identified over 400 emerging technologies that FDA might have to deal with in the future among all the products that we regulate. However, a small number of specific technologies were repeatedly cited as the ones most likely to affect the Agency. Some of these technologies are hybridoma technology, nuclear magnetic resonance imaging and the use of recombinant DNA to produce interferon.

The current study concentrates on veterinary medicine and is intended to determine future prospects for new animal drugs, devices, biologics, feeds and feed additives that are now being developed through new biotechnology methods. So far, over 200 unique products and processes have been identified in the areas of disease diagnosis, prevention and treatment, genetic improvement of animals and others. Over half of the products and processes are in the disease category.

We expect that when this study is completed we will be better equipped, in the Center for Veterinary Medicine, to decide how resources can be most effectively allocated: (1) within the new animal drug review process, and (2) between research and new product review. We will also know more about the direction the Center research should take within the broad area of biotechnology.

4. What has been the effect of research advances on present medical practices? How will present and future technologies impact on the cost of medical care?

Science technology has advanced rapidly during the past decade. New products and processes are being developed constantly. For example, advances in biotechnology will affect the numbers and kinds of new drugs and vaccines available, as well as the methods of producing these products. Advances in biomedical engineering and computerization have resulted in sophisticated new medical devices and diagnostic equipment (e.g., artificial heart, lithotripter, CT scanners, drug delivery systems, etc.). Quite often, new technologies may result in more cost effective treatment modalities. The availability of the lithotripter device for non-evasive treatment of kidney stones is an excellent example. It is estimated that the American public will save $32 million in the first year alone--this is without considering the cost of lost work days had there had to have been surgery. This cost is based on cost differential of $2,000 and 16,000 cases of kidney stones that would be treatable by this new technology. Another good example of this is interferon which is currently under intensive investigation as a chemotherapeutic agent. When initially discovered, interferon was extremely costly to produce, but production of synthetic interferon through rDNA technology has made the material available at a much more reasonable cost. New technology can also increase the cost of care through the availability of more sophisticated diagnostic equipment and more expensive modalities of therapy (e.g., renal dialysis, transplantation, and CT scanners).

5. Will present laboratory and clinical research programs maintain our scientific and technical leadership in the biomedical sciences?

6. Do present policies permit the rapid translation of basic research findings to the development of health products? Is industrial competitiveness being maintained?

It is essential that FDA maintain its scientific and technical excellence in the biomedical sciences to fully support its mission of protecting the public health through programs of research, product approval and post-market surveillance. Without good scientific support, the potential exists for the Agency to be responsible for delays in approving new technologies and products, and/or even the prohibition of these new technologies and products.

While scientific and technical knowledge in the biomedical sciences relies most heavily on the support of institutions such as the NIH, or National Science Foundation (NSF), the FDA has a critical role to play in assuring that the products of new technologies, such as biotechnology, reach the marketplace. Recent efforts of the major regulatory agencies, including the FDA, to assure that the commercial applications of new biotechnology are overseen with clear, consistent regulation is a major step towards maintaining U. S. competitiveness and leadership in this area. Similar cooperative efforts have been initiated at the international level through the OECD (Organization for Economic Cooperation and Development).

FUTURE DIRECTIONS

Basic biomedical research programs are primarily supported by NIH, ADAMHA, and NSF, while it is FDA's responsibility to ensure that products that are the fruits of Government and private sector research are brought to the public in a safe and effective form. Thus, FDA's role in the future of biomedical research can either be that of a barrier or a facilitator of technology transfer.

In order to meet this challenge into the 21st Century, FDA has established a 10-point program to meet the most urgent needs facing the Agency. A description of this program will be provided for the record.

This Action Plan has been divided into objectives and milestones. As of March 31, 1986, 88 percent of the 256 milestones have been started and 49 percent completed. It is anticipated that greater than 90 percent of the Action Plan will be completed by 1988. The plan serves both as a strategy for prudent management and in times of constraint, as a budget for the renewal of the Agency. During the implementation of the plan, we will continue to analyze our priorities to ensure that we fulfill our primary mission.

DISCUSSION

Mr. **Walgren**. Looking at FDA as a whole, how much of it is targeted to or directed toward scientific research as such? Is that 50 percent of our FDA budget, or is that a much smaller portion?

Dr. **Young**. Much smaller. We would have at most, if you counted in the most generous way, $80 million out of our $400 million that would be in some way related to research. But I hasten to add the individuals that are involved in research are also involved in reviewing. For example, the review group in the Center for Drugs and Biologics, the very group that is studying viruses, specifically a hepatitus virus, was shifted to work on AIDS. Subsequently, the group went on to discover the cause of non-A, non-B viral hepatitus, and to demonstrate for the first time it is an AIDS-related virus. If you take all of FDA scientists, and discount their reviewing functions, you would come up with only $80 million. At least 50 percent of their effort is probably related to reviewing.

Mr. **Walgren**. And then you indicated that 2 percent was external?

Dr. **Young**. Yes, sir.

Mr. **Walgren**. That would be 2 percent of the $50 million at that point?

Dr. **Young**. That is correct.

Mr. **Walgren**. Approximately $1 million in external?

Dr. **Young**. Yes. The orphan drug process is about $2.8 million, and that really is a very small amount of extramural grants. But we feel that a conversion factor of 50 percent will be achieved, 50 percent of the grants will go toward medicinals in the country that will eventually be licensed or brought to the market because of this grant program.

Mr. **Walgren**. Almost all of the external is orphan drugs?

Dr. **Young**. A large portion is orphan drugs. We also have some contracts for State collaborative work. Some contracts are specifically designed to look into particular topics whese we have limited expertise in the FDA, such as the contracts with the National Academy of Sciences which helped us review safety data on cyclamates.

Mr. **Walgren**. Do you have any feel for the difference between extramural research and in-house research? Are there quality differences, are there relevant differences or is it, from your point of view, relatively not significant as to where the research is done?

Dr. **Young**. I will give you a more detailed answer to this in the Action Plan, which I will provide to the committee, which is designed to look at our science base (see app. 3). Simply, the answer is this: much of the science that is done intramurally is done on a time-constraint basis. These are things that we need to know immediately. For example, in Illinois this year, there was the largest outbreak of salmonella-induced poisoning related to contamination of milk. At the moment, we have directed a substantial amount of our resources to look at what might be problems in sterilization, in the heat sensitivity of organisms. Those organisms that may be intercellular, do they interact differently if they are free in milk? We need to be able to take our scientists out to the scene of the problem immediately, because we have a major epidemic, if you will, of poisoning of different food products, in dairy products, not related in this sense to anything that can't be controlled, but things that we have discovered recently with different cheeses and milk products. We need to, then, move our scientists to focus on that. It is that type of ability to move scientific efforts to meet the mission of the FDA that cannot be done on extramural grants.

On the other hand, our orphan product program is just the type of program that we want to do primarily extramurally. It is more like the National Institutes of Health system of totally peer-reviewed grants. But the large amount that we do intramurally, in my professional judgment, we would have much more difficulty accomplishing in an extramural way. It doesn't lend itself to the type of research that one assigns to graduate students and postdoctorals, as described so eloquently by Dr. Berg.

Mr. WALGREN. So with that much essentially nonpeer review, but rather mission-directed research, would be that the emphasis of the agency? Are there any generalizations that you can draw about the results of that research?

Dr. YOUNG. Sure.

Mr. WALGREN. Do you see a difference in the fruitfulness, or the degree of innovation that comes from that research? Perhaps this isn't a good question. I am sure there is room for all different kinds of research. Ultimately, we are after a balance, but I am curious about whether or not just looking at the two, whether differences in productivity strike you or differences in quality strike you?

Dr. YOUNG. Let me answer the question on a few different levels. First, I should add for the record that the large majority of FDA research is peer-reviewed. That which is in the Center for Drugs and Biologics has the same peer review as intramural National Institutes of Health research, and because that part of the agency resides on the National Institutes of Health campus, and we use the National Institutes of Health peer review system.

In the case of FDA's National Center for Toxiological Research, we use an extramural peer review system and have a scientific committee look at that. I have detailed that much of these projections, though they are in-house, are peer reviewed because I feel very strongly about the peer review system. The difference is that the research has a much more applied spinoff to it. I have provided for the record a table in excess of 20 pages of discoveries that have come out of FDA-sponsored research, and the table is constructed to give problem solutions and the impact outside of FDA. For example, because modern method was needed to measure the possibility of genetic effects of food chemicals, a veritable transformation technique was developed and this is now widely used in the industry and EPA.

Much of our research is on methods; another portion on risk assessment. I have documented in excess of 20 pages, if you will, that will give you a feeling for that. It is not a better type of research. I would submit that bright minds are needed just as much in the fascination of tracing down cyanide deaths, if you will, or food poisoning, or as we do in some international cases, of major problems of food poisoning. You need just the same type of brilliance in during that, as in NIH research, but it is a different type of research.

We use peer review of outstanding scientists. One of our biggest problems is recruiting outstanding scientists because, regrettably, very little is known about FDA and the FDA science base. The largest cluster of individuals involved in applied nutrition in the world is in FDA. We set the standard for the World Health Organization, the Pan American Health Organization, and in the other food organizations, and we train inspectors and food sanitarians around the world. But I must also admit that before coming to FDA, I had no real idea of the scope and magnitude of its impact.

Mr. **Walgren**. Can you make any suggestions on effective transfers or development of basic research into something that is evident of near to applied nature, because all of us are interested in the findings of research that we do with tax money, becoming useful to the society, as opposed to just an idea?

Dr. **Young**. Sure.

Mr. **Walgren**. Can you see things in FDA that are missing in other parts of the scientific effort that perhaps we, as a Congress should be thinking bout, trying to add to other parts of the effort?

Dr. **Young**. I would give you three concrete examples that may be of help. I concur that basic research is the citadel and foundation of all that we build; I am taking that as an assumption, and now going on to our very important question.

We have a poor interlock between discoveries on the one hand and applications on another. Part of this is the fault, in my opinion, of the way we bring products to the marketplace. For example, as little as $25 million invested in the drug approval process, would provide a decrease in the time of the approval process of 10 to 12 months. If you owned a company and were desperately trying to bring a technological product on line, you would have $90 million of capital invested interest free for an additional 13 months.

We feel that one way to handle this is to have an application processing fee where you, as the beneficiary would pay upfront. Under those circumstances, we would be able to add a couple of hundred reviewers, facilities, and technology—our word processing equipment is state-of-the-art 1953—it doesn't exist. But an application, 500,000 pages, is twice as tall as I am—quite a mound of paper and we don't have this on a computerized system that we can deal with. These types of obstructions could be corrected by approval of a user fee, or an application fee. That would, in contrast to burdening the Federal Government with an already hemorrhaging deficit, would bring it back to the individuals that benefit from it and would provide an access, if you will, toward a more rapid technology approval.

The reason it takes 25 months instead of 12 is that we can't get to the applications, not that we are sitting around deliberating such decisions.

The second area is in the field of risk assessment. We know little about the various molecular activities of hazardous compounds as they impact on human beings. So we make these huge extrapolations from animals to human beings. There are difficulties in regards to the way we deal with our epidemiology. So, authorizations in regulatory agencies therefore are deliberately conservative. I would submit, for FDA and EPA, and USDA, particularly at this critical time of biotechnology development, that if we don't have a good assessment of risk, we will be too conservative. We will drive overseas an industry that is extraordinarily important; particularly since in the United States, unlike any other nation in the world, drugs and biologicals which are not yet approved, though which would have clinical value, cannot be exported. So, one exports instead the technology, or exports the jobs to other countries. Here again, is a bill that could be brought forward by the Congress that would make a difference.

Another area—and here I must talk as an old dean on the stump, if you will, I will sound like Dr. Berg on—is raising money from the local industries to match with my National Institutes of Health grants to build facilities. I can't do that at FDA, or at least I haven't figured out yet how to do it. One of our most critical areas is in helping the farmer by looking at the impact of some of the drugs, and some of the medicinals that are going into animals. For years, we have had our microbiologists from the Center for Veterinary Medicine in an old WPA 1939 remodeled chicken coop and our barns were in such poor repair that we could only get one that was down at the bottom of the hill. We lost 8 months of research when there was a flood, and the feed that was being used to test aflatoxin and its migration into milk was contaminated by the runoff from the hog pens up the hill, and we had to scrap that study.

We have petitioned, in the only way that FDA knows how, for a number of years to build the necessary type of facilities. It is the same argument that Dr. Berg was raising, but I think in regulatory agencies, if we don't have the facilities to do the experiments on time, it only makes it very difficult to bring the proper health protection to the American people, and I would urge that Congress look at this as well, as a significant portion. We need the capital, but I cannot raise it, as I said, in the old dean on the stump trick.

Mr. WALGREN. Thank you.

Mr. PACKARD. What type of research projects are done at the FDA?

Dr. YOUNG. I will give you a few examples of those and I gave many in the testimony.

One type of research that is very important is the analysis of artificial systems that would analyze a mockup system of blood flow. In your region of the country, there is a corporation that produces heart valves, artificial heart valves, and we need to be able to test in an actual flow model some of those structures, particularly to look for strain.

We also look at artificial joints, if you will, because all of these have to be approved by the FDA.

On the other hand, we would look at the development of vaccines, whose development is extraordinarily critical. All of those are approved by FDA. Therefore, right now we are looking at and evaluating some of these vaccines.

In the field of foods we are looking at contaminants and are developing probes for the particular type of organisms that are commonly found in food and food poisoning. So we want to be able to look at salmonella infusions very rapidly, and be able to hybridize with DNA-related probes so we can pick these out. The same in soft cheeses, which is a problem at this point.

Analytical methods. The work of Frickey in Cincinnati, spending years trying to look at most ultrasensitive methods for heavy metal detection, enabled us to react to the Tylenol crisis. It is these types of research that is very important for FDA.

Mr. **Packard**. So FDA research is primarily oriented toward their mission?

Dr. **Young**. Absolutely.

Mr. **Packard**. To regulate, to evaluate and to make decisions on other research?

Dr. **Young**. That is right. We do not repeat the types of studies that are in the National Institutes of Health or NSF.

Mr. **Packard**. Then what do you consider then as your primary and fundamental function? Is it in doing this type of research, or is it primarily in the review and evaluation and regulation of products and materials?

Dr. **Young**. Our primary function is to protect the public health, the citizenry in relation to food, drugs, devices, cosmetics. In order to do that, we have multiple functions. One is a reviewing function, one is a regulatory function, and the other is to provide the scientific base on which we can do the other two, because no one else does this type of research. We have to include this in our mission in order to serve the public. In the absence of that, for example, if we were not doing research, biotechnology-related, I could assure that it would have taken much longer to bring tests on line. If we were not working in drugs in this way, and testing some of the compounds, we would not be able to approve new investigational drug applications in 5 days, if you can imagine. That is as fast as you can turn the paper around. So our intimate involvement in it is essential for our regulatory role.

Mr. **Packard**. How in that research role that you do, your own research that is conducted at FDA, how is that monitored in terms of quality control of the research, and do you have an in-house, or some type of external peer review systems of your own research project?

Dr. **Young**. Yes, sir; I have detailed that in the testimony and we have both of those.

In regard to the in-house research, we have peer review systems analogous to the National Institutes of Health program in which applications are reviewed in that fashion. In addition to that, we do have a committee within FDA that looks at the research in relation to our mission, we have to give some degree of relevance for this research, because it really is related to crises that are going on, or projected crises. So, we do take both into consideration, we do have very extensive peer review and programmatic review within FDA. To do otherwise would not be good policy.

Mr. **Packard**. Among scientists—probably maybe this is only my perception—probably the most acute sense of protection and pride of authorship or ownership of ideas, particularly novel and unique activity and innovative ideas, how do you protect your scientists from this inherent bias or inherent jealousy of information and research that is being done to the point where they can evaluate and recommend regulation on a fair and equitable basis, rather than from their own perhaps biased view, being scientists themselves and performing scientific activities within the agency?

Dr. YOUNG. With great difficulty, but the strongest defense is having outstanding scientists. Our scientists, like scientists in a university, do participate in the publication in peer review journals, we have them attend meetings, but the biggest protection is to recruit the best. We have a different disincentive though, because our scientists after a few years, particularly those involved in regulation, and can be seduced into industry at four times their salary. The repeated recruitment of bright young people is very hard. We don't have the type of milieu that the National Institutes of Health does. I am glad I never saw the Parklawn Building before I was recruited as Commissioner. I may have run away.

Mr. PACKARD. Do you see scientists perform, within FDA, perform research activities that is earmarked toward their role as evaluators and regulators? Do you see any projects, or any competitiveness, between that which they are evaluating, and that which they themselves are doling in terms of research?

Dr. YOUNG. No; we do not allow scientists to both work on anything that is directly related to a particular sponsor, and review that sponsor's application. If there was any relationship between the industry and the scientist it would be a conflict of interest in that area. We try to protect it by having an individual knowledgeable in the field. If you are a person dealing with biotechnology, with a base in the field worked of bacilli biotechnology, that fundamental base then would be widened when one applied to the wide variety of biomedical aspects of a project that one is reviewing. So we do not see a conflict there.

Since we are reviewing things that are going to the marketplace, and are very applied, our own research is not threatened in that fashion as a competitor, if you will. If I have understood your question correctly, we do not see it as competition.

Mr. PACKARD. In the role of protecting the public, would you say most products that you, and devices that you have to evaluate, and ultimately to regulate, that there is a balance between public good and public protection?

Dr. YOUNG. Yes.

Mr. PACKARD. Do you have a formula, do you have a—what is your system of trying to make those very difficult choices, because every product has got—well not every, but most I have to assume is being marketed on the basis that it has got some fundamental public good that is marketable, and at the same time there are some hazards that could be associated with it.

Dr. YOUNG. Sure.

Mr. PACKARD. Complications or whatever. How do you evaluate and ultimately make your regulatory decisions?

Dr. YOUNG. The basis of a regulatory decision is as follows: an application to be approved must be approved on its safety and its effectiveness. In the drug approval process, which is the easiest for me to explain for you, if you were the director of a corporation, you would conduct preclinical trials for a number of years before submitting the compound to FDA with a request for an investigational new drug application. If, FDA judged, after looking at your data, that it was safe to begin with human trials, we would approve you for a very limited trial on 10 to 20 people, based on our scientific analysis of your data. After that result was finished you would come back to FDA in one form or another and you would undertake a trial of 200 individuals. When that data were collated, you would come at what we call now the end of the phase II, the conference, and you would meet with FDA officials and would design the last study, which would now involve 2,000 to 5,000 individuals. A dialog would occur on the likely to be safety conditions and efficacy conditions. Then you would do the final double-blinded trial, if you will, on clinical effectiveness. After that, you would package a new drug application, and it would come for review at FDA. A conference would occur to discuss the claims for the drug and the advice to be given to the physician community. We have, after that, a market survey and we have within our group again, if you will, another research type project where we analyze adverse reporting coming in. If there is a serious adverse reaction to the drug, we can remove it from the market. We try to balance in one way the very seriousness of the disease with some of the efficacy and safety aspects, but we don't have a particular formula.

For example, in AIDS, we know that the disease is 100 percent fatal. Therefore, a drug that may have a few more side effects might be brought into a clinical trial because the disease is known to lead to death. On the other hand, if a disease was a chronic disease, for example, arthritis, where there may be other modes of therapy, one would look at a nonsteroidal drug that would be anti-inflammatory. The efficacy and safety and long-term studies would be much greater because one usually does not die of arthritis.

So, there is a balance, not a critical formula, but to us, the single most important person is the medical reviewer. That is why one of our emphases in the Action Plan as we bring it forward, is to bring a larger number of medical reviews of the very type that Dr. Berg described. It is that judgment of qualitative risk/benefit that we need as we approve drugs on the basis of safety and efficacy.

Mr. PACKARD. So, your review process is flexible where there can be some fast tracking and others could take years?

Dr. YOUNG. Yes, sir; we do that. In the case of AIDS, we have pledged to act on these drugs with an approval or nonapproval in less than 180 days.

Mr. WALGREN. Mr. Brown.

Mr. BROWN. No questions.

Mr. WALGREN. Well, on behalf of the group, thank you very much, we appreciate your bringing resources to us and we look forward to talking to you.

Dr. YOUNG. Thank you. I would be glad to handle any followup questions from the committee.

[Questions and answers for the record follow:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

December 2. 1986

Note to: Kiki Hellman
Science Policy Task Force
Committee on Science and Technology

Subject: Followup questions on the hearing
on biomedical research,
April 24, 1986.

As you requested, attached are FDA responses to the followup questions from the hearing on biomedical research on April 24, 1986. Per your conversation with Dr. Danello, we have not prepared a response to question #5.

If I can be of any further assistance, please let me know.

Jo Anne C Marrone
JoAnne C. Marrone
Office of Legislative Affairs
Food and Drug Administration

Question #1

Is it possible to form a strategy leading to greater emphasis on the development of cost-saving research and technology in contrast to the rapid increase in health care costs as a result of the high technology used in current medical practice?

Answer

We can certainly understand the Task Force's concern regarding the high cost of health care and the impact these costs have on the ability of people to cope with their illnesses and meet other expenses as well.

However, issues relative to cost are not the purview of the Food and Drug Administration. The Federal Food, Drug, and Cosmetic (FDC) Act, which we administer, contains no provision authorizing us to establish prices charged for any of the products we regulate. Our jurisdiction under the Act, and other related laws, is directed primarily toward ensuring that the Nation's pharmaceutical, biological, medical device and radiological products are safe and effective, that the food supply is safe and nutritious, and that all products are properly labeled.

This may be an issue that is more properly addressed at the Department level, perhaps by the National Center for Health Services Research and Health Care Technology Assessment.

Question #2:

From your perspective, is government targeting of research for certain health problems desirable? If so, what should be the balance between support of targeted versus non-directed programs? What criteria should be used in the decision-making process and who should be involved?

Answer #2

I understand that your question does not relate directly to the Food and Drug Administration (FDA) because, in a sense, our research is in fact, already targeted. However, I would like to discuss briefly the value of targeted research as it does relate to FDA. In any discussion about research, it is important to understand the distinction between the goals of FDA scientific research and those of other research institutions. As I mentioned in my testimony at the hearing, research undertaken by FDA is often unique and very specialized in that it is targeted to support the regulatory mission of the Agency. For example, FDA's research must have the capacity to develop quick, accurate, sensitive and reproducible methods which can be applied in response to public health emergencies. This capability was most strikingly demonstrated during the cyanide tampering incidents when FDA scientists developed a technique which could identify precisely the manufacturing origin of the cyanide. Other examples of how our research efforts support our regulatory mission are contained in my testimony.

It is essential that our research base continues to be targeted in order to provide sound support for FDA's regulatory activities. As I stated in my testimony, because the major scientific fields are advancing rapidly. our own research must keep pace with that of academia and industry. The relatively untargeted fundamental research that NIH supports is also very important and necessary for our success because it provides a strong foundation of basic scientific knowledge on which to base some of our more targeted research. Without such basic research our targeted studies could not succeed.

As I also discussed in my testimony, because of its unique relationship to regulatory actions, most of FDA's research is carried out in each of our individual centers. The research planning activities of each center are part of a larger planning program for the entire Agency. However, research projects identified under this program are not static and change as the priority issues for the Agency change, depending upon the types of new products being generated by industry and academia or contemporary crises, or important public health issues such as AIDS. It is, therefore, important that the individual centers continue to have input into the decisionmaking process and that we have the flexibility to reassess our research programs as the need arises.

Question #3:

You indicated that there is a critical need for maintaining a strong biomedical science base in FDA. Is progress being jeopardized because of stringent fiscal policies? Is it difficult to attract and retain talented young researchers because of such policies? What suggestions can you offer in this regard?

Answer

As I mentioned in my testimony, much thought is being given to the problems of recruitment and retention of scientific personnel. The need to recruit and retain young scientists becomes apparent when one realizes that the average age of FDA scientists is now 44. The management portion of the Action Plan thus calls for significant improvements in the areas of career advancement, laboratory research programs and science base. Clearly, our personnel are our single most important resource. FDA's ability to review and regulate new products on the cutting edge of technology as well as conduct the research that provides the foundation for our activities requires that we employ excellent scientific personnel. We must maintain an atmosphere in which our scientists can actively contribute to their professions and the regulatory mission of the Agency as well. This is probably the most important issue facing us. As workload increases we have had to scale back for scientists commitment to the development of new knowledge, and have them merely focus on the review process for new products. Unless FDA scientists remain current with their fields of expertise through individual research, by interacting with colleagues and superiors within the Agency, and by identifying new problems that need attention, they will not be able to continue to approve products with a certain knowledge of contempory science.

Recognizing that the Agency is dependent upon the maintenance of a strong scientific program, the Action Plan calls for the undertaking of a number of science-related management initiatives. To attract and maintain scientists, career ladders for scientists will be evaluated with particular attention directed at the adequacy of laboratory resources, recognition of outstanding research, and the establishment of a peer review system for intramural research scientists staff fellowship programs. Particular emphasis will be directed toward cooperative FDA/university interaction, "mini" leaves of absence for scientific and medical personnel as a function of duration of service and career plans, collaborative research, and interchange between field and headquarters scientists. Additionally we must recongnize that salaries for our scientists must be competitive with the academic community.

Question #4:

It has been mentioned that the NIH program has certain attributes which could be applied in the biomedical research programs of other federal agencies. In your view, what would be the relative advantages and disadvantages of the NIH-like research program at the FDA?

Answer

The research programs at the NIH and the FDA are actually complementary. While the NIH programs support less targeted basic biomedical research, FDA programs support research which utilizes that basic information to confront specific, targeted, public health problems.

As was discussed in my testimony, FDA's research mission is unique. The Agency's research must suport both short-term goals associated with the Agency's ability to react quickly to public health emergencies and longer term goals associated with the Agency's ability to ensure the safety and effectiveness of new medical products and the quality of the Nation's food supply. Thus, our research is directed at elucidating Public Health programs and providing solutions that will lead to the resolution of these problems.

Because of its unique relationship to regulatory actions, most of FDA's research is approximately carried out in-house. The research activities of the individual centers are described in detail in my testimony. The relevence of this type of research program becomes more evident as one understands the programs of these individual centers.

One notable exception is our grants program for orphan products. We are especially proud of this program which fosters the development of products for rare diseases and conditions. This program is intended to support the development of products prior to the submission to FDA of an application for marketing approval. In this respect, our orphan products development program already stands on a broad base of NIH-supported knowledge and helps provide a gateway to marketing for products that are critically needed by relatively small populations.

One aspect of the NIH which provides a unique advantage is the actual physical environment for the scientists. The campus-like arrangement of research institutes encourages a spirit of collegiality and collaboration which enhances the level of scientific innovation and advancement. In fact, FDA's Center for Drugs and Biologics, has benefitted tremendously from its presence on the NIH campus and its proximity to a wide variety of scientific expertise. In contrast other centers have suffered from isolation from the NIH campus or equivalent centers of learning and research.

One area where FDA utilizes a system similar to NIH is in the use of scientific advisory committees to continue to provide outside technical advice on certain difficult scientific issues associated with particular product applications. The Agency views these types of review as critical to maintaining high standards of research and as a part of its Action Plan, plans to enhance the use of scientific peer review within the Agency.

Clearly there are advantages to each program. The goal is to serve the public health. Both Agencies are committed to maintaining a strong science base as the means to this end.

Mr. **Walgren**. Dr. Neaves, dean of the Graduate School of Biomedical Sciences, University of Texas Health Science Center.

STATEMENT OF DR. WILLIAM B. NEAVES, DEAN, SOUTHWESTERN GRADUATE SCHOOL OF BIOMEDICAL SCIENCES, THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT DALLAS, DALLAS, TX

Dr. **Neaves**. Chairman, members of the committee, I am William B. Neaves, Ph.D., dean of Southwestern Graduate School of Biomedical Sciences at the University of Texas Health Science Center at Dallas. I am here to tell you about an innovative approach in technology transfer based in Dallas.

Technology transfer is the process of getting knowledge about better ways of doing things and about potential new products out of university laboratories and into the commercial world. It is not just good for business and industry. Without technology transfer, some of the most successful university research is incomplete. As medically useful technologies emerge in university research laboratories, many of them cannot be translated into public benefit without industrial collaborators who can develop, manufacture, and market products.

At the University of Texas Health Science Center at Dallas, we have had limited success in the past in attracting industrial collaborators to commercialize the results of our research. Since we lack a network of business contacts within the medical products industry, we have waited passively for commercial interests to learn of our work through their own efforts.

Sometimes failure has resulted from our naive reliance on large corporations whose investment in an established and profitable product line mitigates against timely introduction of a competing innovation. For example, our patented process of treating medical plastics to prevent blood clots without using heparin was rejected by a large manufacturer of intravenous catheters for the stated reason that the corporation made more money selling heparin to prevent blood clots in catheters than they did selling the catheters themselves.

Most often, failure results from a funding gap between basic research and product development. Many businesses are unwilling to sponsor a project until its commercial potential has been clearly demonstrated, and such a demonstration is often outside the scope of basic research. For example, basic research funded on our campus by the National Institutes of Health recently yielded a new diagnostic test for susceptibility to juvenile diabetes, but potential commercial sponsors have been reluctant to carry the project forward without evidence of how the test could be simplified and used in a kit suitable for hospitals and clinics. The latter goal is, of course, outside the mission of a National Institutes of Health-funded basic research grant. Thus, the project has languished in a gap between National Institutes of Health-sponsored basic research and industry-sponsored development.

Because of frustrations such as these, we have begun a new experiment in technology transfer. The centerpiece of the experiment is a private, for-profit corporation called Dallas Biomedical Corp.

Created with $12 million of investment capital, its purpose is to make money for its stockholders by increasing the yield and accelerating the transfer of commercially promising results of basic biomedical research conducted at the University of Texas Health Science Center at Dallas. To achieve this purpose, it was designed to address the perceived reasons for poor success in our earlier efforts at technology transfer. Specifically, Dallas Biomedical Corp. was structured to provide: first, a network of contacts in the medical products industry through its professional staff, its investors, and its board of directors; second, a wider range of commercialization options, including formation of new start-up companies, limited partnerships, joint ventures, and sale of technology, as well as traditional patent licensing to established corporations; and third, a source of funds to carry mature projects beyond basic research toward product development.

Three independent but coincident and convergent interests conspired in the creation of Dallas Biomedical Corp. The first was the university's desire to commercialize the results of its research more effectively and its perception that outside help was needed.

The second was the desire of the Dallas business community to diversify the local economy by fostering an industry based on biomedical technology. This desire materialized in the Dallas mayor's biotechnology task force appointed by Mayor A. Starke Taylor, and chaired by C. Vin Prothro, a Dallas business leader and venture capitalist.

The third was an invitation from the John A. Hartford Foundation for the University of Texas Health Science Center at Dallas to compete with the Nation's other leading centers of biomedical research for a grant to develop a model technology transfer program. The Hartford Foundation had identified the funding gap between basic research and commercial sponsorships of product development as a major impediment to technology transfer at the Nation's medical schools.

The Hartford Foundation catalysed the creation of Dallas Biomedical Corp. through its challenge to devise a technology transfer plan that would fill the funding gap. The response of the University of Texas Health Science Center at Dallas and the mayor's biotechnology task force was shaped by each group's motives. For the University of Texas Health Science Center at Dallas, the principal motives were, first, to ensure that potentially beneficial results of biomedical research do not languish in the laboratory; second, to provide additional incentive for inventive faculty scientists to remain in the university; and third, to increase the income earned by the university through commercialization of its technology.

For the mayor's technology task force, the principal motives were, one, to foster development of the biomedical technology industry in Dallas; two, to create new investment opportunities for the Dallas business community; and three, to generate direct economic return for investors in the new corporation.

Dallas Biomedical Corp. was designed to be simple, small, independent, and safe.

Keep it simple. Dallas Biomedical Corp. is a for-profit corporation financed through the private sale of stock. Stockholders elect a board of directors who hire a president to run the company. Dallas

Biomedical Corp. invests in development-stage projects at a top-quality center of biomedical science. Dallas Biomedical Corp. assumes all business management rights in sponsored projects and splits profits 50/50 with the university. The university splits its share of the profit 50/50 with the faculty scientists responsible for the project.

Keep it small. Dallas Biomedical Corp., together with matching funds from the Hartford Foundation, will have $1.2 million per year to invest in development-stage projects at the University of Texas Health Science Center at Dallas. When added to the current commercial sponsorship at the University of Texas Health Science Center at Dallas, the total represents a desirable level of commercially-sponsored applied research in comparison to the current $50 million annual budget for basic research at the university. Tailoring Dallas Biomedical Corp.'s expenditures to maintain a 15:1 ratio between basic and applied research on campus was intended to avoid: one, distorting the traditional and appropriate commitment of the university to basic research; and two, making poor investments by throwing too much money at too few suitable projects.

Keep it independent. Dallas Biomedical Corp. cannot be controlled by the University of Texas Health Science Center at Dallas. No one at the university can be a stockholder, officer, or director of Dallas Biomedical Corp. Because of matching funds from the Hartford Foundation, Dallas Biomedical Corp. has an incentive, in addition to its business strategy, to invest at the University of Texas Health Science Center at Dallas. However, Dallas Biomedical Corp. is entirely free to invest at other institutions. Similarly, the University of Texas Health Science Center at Dallas is free to place any of its projects with other commercial sponsors. Hence, the relationship between Dallas Biomedical Corp. and the University of Texas Health Science Center at Dallas has been structured to preserve competition and to ensure that funding decisions are made for sound business rather than academic reasons.

Keep it safe. Dallas Biomedical Corp. cannot lose its investors' capital. It has been capitalized with $12 million in privately sold stock. This corpus has been placed in conservative interest-bearing securities that will yield at least $900,000 a year. Up to $300,000 per year can be used for operation, leaving $600,000 for project funding to match the $600,000 annual Hartford Foundation grant over each of the next 5 years. Stockholders can retrieve their capital after 5 years if they feel the corporation is not meeting its investment objective.

Dallas Biomedical Corp. has been deemed unique by consultants from the Battelle Institute, who served the Dallas mayor's biotechnology task force, and by the staff and trustees of the Hartford Foundation, who selected it for their award from among competing proposals submitted by other leading research universities across the country. Unique features of Dallas Biomedical Corp. include the following: one, it is the first investment-fund company created by a city's business and academic communities for the purpose of taking early development-stage projects from biomedical research laboratories into the commercial marketplace; two, although it is oriented toward high-risk projects that need more development work before commercial potential is certain, it preserves its investors' capital; three, its business strategy concentrates on one academic institution as the source of innovations covering a broad range of biomedical science; and four, it emphasizes flexible use of commercialization vehicles, including new start-up companies that enable stockholders and the university to benefit from equity participation.

Dallas Biomedical Corp. is not a new way of funding basic biomedical research. Instead, it is a device to improve the efficiency and yield of the technology harvest from basic research funded by other sources, principally the National Institutes of Health. Were it not for the $36 million per year in Federal support of basic research at the University of Texas Health Science Center at Dallas, plus another $14 million per year from private sources like the American Heart Association, the American Cancer Society, and Howard Hughes Medical Institute, there would be no reason for Dallas Biomedical Corp. to exist.

Dallas Biomedical Corp. is an experiment that has just begun. Like any experiment, it can either succeed or fail, but the verdict will be years in the making.

Short-term success. Success over the first 5 to 7 years would be reflected in income from technology sales or joint ventures, some royalty from patent licenses, and perhaps one or two viable new start-up companies in Dallas, with total profits or equity returns sufficient to sustain cofunding after expiration of the Hartford Foundation grant. Even in a successful scenario, however, one would expect more than half of the 20 to 30 projects funded during this period to have been failures. Significant income would be expected from only one or two projects.

Long-term success. Success over a 10- to 20-year period would be reflected in notable profits for investors and the university, establishment of a local biomedical technology industry, and returns from at least one commercial winner sufficient to fund some basic research in addition to sustaining project cofunding. A continuing relationship between the University of Texas Health Science Center at Dallas and Dallas Biomedical Corp., and possibly with competitive emulators of Dallas Biomedical Corp., could be anticipated.

Consequences of success. Success of DBC is not without risk to the university. Should Dallas Biomedical Corp. be lucky enough to produce one or two really big commercial winners, Dallas Biomedical Corp. itself, as well as emulators, might wish to provide the University of Texas Health Science Center at Dallas with more commercial sponsorship than required to fill the legitimate funding gap. Although such a problem should be self-correcting in the long run, since extravagant development funding should yield poor returns for investors, in the short run it could distort the appropriate preponderance of basic versus applied research funding in the university setting. Although the university is free to reject funding proposals that threaten this balance, whether it would do so is uncertain.

Failure. Investor satisfaction with Dallas Biomedical Corp. is required for the corporation to survive beyond its first 5 years of operation. This does not mean that Dallas Biomedical Corp. must yield profits by then, but it does mean that exciting projects must be progressing toward predictable returns. Otherwise, Dallas Biomedical Corp. will dissolve, its capital will return to the investors, and the University of Texas Health Science Center at Dallas must again rely, at least temporarily, on conventional technology transfer mechanisms.

Consequences of failure. If this experiment succeeds, no one will care if the credit belongs more to the quality of the university's research or more to the business acumen of Dallas Biomedical Corp. On the other hand, failure might well damage the respect and prestige the university enjoys in the Dallas community. By embarking on this venture, the University of Texas Health Science Center at Dallas has exposed itself for the first time to community judgment according to business rather than academic standards. This is the principal risk assumed by the university.

The Dallas mayor's biotechnology task force and the University of Texas Health Science Center at Dallas have structured Dallas Biomedical Corp. to exploit and help manage the commercial opportunities arising from a mature biomedical institution that spends more than $50 million per year on basic research. Dallas Biomedical Corp. has also been designed to minimize the consequences of failure, in that investors will not lose their capital and the university is free to use other commercialization vehicles. As a result, failure of Dallas Biomedical Corp. need not discourage the university and the Dallas business community from embarking on new experiments in technology transfer that might benefit from experience gained in the present venture.

These precautions notwithstanding, the University of Texas Health Science Center at Dallas, the Dallas Biomedical Corp. investors, and the Hartford Foundation believe Dallas Biomedical Corp. has an excellent chance of meeting all established criteria for its success, namely: (1) generation of economic return for its investors; (2) creation of new investment opportunities for its stockholders; (3) diversification of the Dallas economy; (4) translation of research results into public benefit; (5) retention of creative faculty scientists in the university; (6) addition of income to the university; and(7) recognition as a model program of technology transfer.

Thank you for the opportunity to prove testimony. I would be pleased to answer any questions that the committee might have.

[The prepared testimony of Dr. Neaves follows:]

TESTIMONY ON TECHNOLOGY TRANSFER FOR THE COMMITTEE ON SCIENCE AND TECHNOLOGY - April 24, 1986

Mr. Chairman, I am William B. Neaves, Ph.D., Dean of Southwestern Graduate School of Biomedial Sciences at The University of Texas Health Science Center at Dallas. I am here to tell you about an innovative approach in technology transfer based in Dallas.

Technology Transfer

Technology transfer is the process of getting knowledge about better ways of doing things and about potential new products out of university laboratories and into the commercial world. It is not just good for business and industry. Without technology transfer, some of the most successful university research is incomplete. As medically useful technologies emerge in university research laboratories, many of them cannot be translated into public benefit without industrial collaborators who can develop, manufacture, and market products.

Reasons for Limited Success in Dallas

At The University of Texas Health Science Center at Dallas (UTHSCD), we have had limited success in the past in attracting industrial collaborators to commercialize the results of our research. Since we lack a network of business contacts within the medical products industry, we have waited passively for commercial interests to learn of our work through their own efforts.

Sometimes failure has resulted from our naive reliance on large corporations whose investment in an established and profitable product line mitigates against timely introduction of a competing innovation. For example, our patented process of treating medical plastics to prevent blood clots without using heparin was rejected by a large manufacturer of intravenous catheters for the stated reason that the corporation made more money selling heparin to prevent blood clots in catheters than they did selling the catheters themselves.

Most often, failure results from a funding gap between basic research and product development. Many businesses are unwilling to sponsor a project until its commercial potential has been clearly demonstrated, and such a demonstration is often outside the scope of basic research. For example, basic research funded on our campus by the National Institutes of Health (NIH) recently yielded a new diagnostic test for susceptibility to juvenile diabetes, but potential commercial sponsors have been reluctant to carry the project forward without evidence of how the test could be simplified and used in a kit suitable for hospitals and clinics. The latter goal is, of course, outside the mission of an NIH-funded basic research grant. Thus, the project has languished in a "gap" between NIH-sponsored basic research and industry-sponsored development.

An Experimental Solution to Previous Problems

Because of frustrations such as these, we have begun a new experiment in technology transfer. The centerpiece of the experiment is a private, for-profit corporation called Dallas Biomedical Corporation

(DBC). Created with $12 million of investment capital, its purpose is to make money for its stockholders by increasing the yield and accelerating the transfer of commercially promising results of basic biomedical research conducted at UTHSCD. To achieve this purpose, it was designed to address the perceived reasons for poor success in our earlier efforts at technology transfer. Specifically, Dallas Biomedical Corporation was structured to provide:

(1) a network of contacts in the medical products industry through its professional staff, its investors, and its board of directors,

(2) a wider range of commercialization options including formation of new start-up companies, limited partnerships, joint ventures, and sale of technology as well as traditional patent licensing to established corporations, and

(3) a source of funds to carry mature projects beyond basic research toward product development.

Who Created DBC

Three independent but coincident and convergent interests conspired in the creation of Dallas Biomedical Corporation. The first was the University's desire to commercialize the results of its research more effectively and its perception that outside help was needed.

The second was the desire of the Dallas business community to diversify the local economy by fostering an industry based on biomedical technology. This desire materialized in the Dallas Mayor's Biotechnology Task Force appointed by Mayor A. Starke Taylor and chaired by C. Vin Prothro, a Dallas business leader and venture capitalist.

The third was an invitation from the John A. Hartford Foundation for UTHSCD to compete with the nation's other leading centers of biomedical research for a grant to develop a model technology transfer program. The Hartford Foundation had identified the funding gap between basic research and commercial sponsorship of product development as a major impediment to technology transfer at the nation's medical schools.

Why DBC was Created

The Hartford Foundation catalysed the creation of Dallas Biomedical Corporation through its challenge to devise a technology transfer plan that would fill the funding gap. The response of UTHSCD and the Mayor's Biotechnology Task Force was shaped by each group's motives. For UTHSCD, the principal motives were:

(1) to ensure that potentially beneficial results of biomedical research do not languish in the laboratory,

(2) to provide additional incentive for inventive faculty scientists to remain in the University, and

(3) to increase the income earned by the University through commercialization of its technology.

For the Mayor's Biotechnology Task Force, the principal motives were:

(1) to foster development of the biomedical technology industry in Dallas

(2) to create new investment opportunities for the Dallas business community, and

(3) to generate direct economic return for investors in the new corporation.

How DBC was Structured

Dallas Biomedical Corporation was designed to be simple, small, independent, and safe.

Keep it simple - DBC is a for-profit corporation financed through the private sale of stock. Stockholders elect a board of directors who hire a president to run the company. DBC invests in development-stage projects at a top-quality center of biomedical science. DBC assumes all business management rights in sponsored projects and splits profits 50/50 with the University. The University splits its share of the profit 50/50 with the faculty scientist responsible for the project.

Keep it small - DBC, together with matching funds from the Hartford Foundation, will have $1.2 million per year to invest in development-stage projects at UTHSCD. When added to the current commercial sponsorship at UTHSCD ($2.0 million per year excluding routine drug testing contracts), the total (i.e., approximately $3.2 million) represents a desirable level of commercially-sponsored applied research in comparison to the current $50 million annual budget for basic research at the University. Tailoring DBC's expenditures to maintain a 15:1 ratio between basic and applied research on our campus was intended to avoid:

(1) distorting the traditional and appropriate commitment of the University to basic research, and

(2) making poor investments by throwing too much money at too few suitable projects.

Keep it independent - DBC cannot be controlled by UTHSCD. No one at the University can be a stockholder, officer, or director of DBC. Because of matching funds from the Hartford Foundation, DBC has an incentive, in addition to its business strategy, to invest at UTHSCD. However, DBC is entirely free to invest at other institutions. Similarly, UTHSCD is free to place any of its projects with other commercial sponsors. Hence, the relationship between DBC and UTHSCD has been structured to preserve competition and to ensure that funding decisions are made for sound business rather than academic reasons.

Keep it safe - DBC cannot lose its investors' capital. It has been capitalized with $12 million in privately sold stock. This corpus has been placed in conservative interest-bearing securities that will yield at least $900,000 per year. Up to $300,000 per year can be used for operation, leaving $600,000 for project funding to match the $600,000 annual Hartford grant over each of the next five years. Stockholders can retrieve their capital after five years if they feel the corporation is not meeting its investment objective.

Why DBC is Unique

Dallas Biomedical Corporation has been deemed unique by consultants from the Batelle Institute, who served the Dallas Mayor's Biotechnology Task Force, and by the staff and trustees of the Hartford Foundation, who selected it for their award from among competing proposals submitted by other leading research universities across the country. Unique features of DBC include the following.

(1) It is the first investment-fund company created by a city's business and academic communities for the purpose of taking early development-stage projects from biomedical research laboratories into the commercial marketplace.

(2) Although it is oriented toward high-risk projects that need more development work before commercial potential is certain, it preserves its investors' capital.

(3) Its business strategy concentrates on one academic institution as the source of innovations covering a broad range of biomedical science.

(4) It emphasizes flexible use of commercialization vehicles, including new start-up companies that enable stockholders and the university to benefit from equity participation.

What DBC is Not

Dallas Biomedical Corporation is not a new way of funding basic biomedical research. Instead, it is a device to improve the efficiency and yield of the technology harvest from basic research funded by other sources, principally the National Institutes of Health. Were it not for $36 million per year in Federal support of basic research at UTHSCD, plus another $14 million per year from private sources like the American Heart Association, the American Cancer Society, and the Howard Hughes Medical Institute, there would be no reason for DBC to exist.

Where DBC Could Lead

Dallas Biomedical Corporation is an experiment that has just begun. Like any experiment, it can either succeed or fail, but the verdict will be years in the making.

Short-term success - Success over the first 5-to-7 years would be reflected in income from technology sales or joint ventures, some royalty from patent licenses, and perhaps one or two viable new start-up companies in Dallas, with total profit or equity returns sufficient to sustain co-funding after expiration of the Hartford grant. Even in a successful scenario, however, one would expect more than half of the twenty-to-thirty projects funded during this period to have been failures. Significant income would be expected from only one or two projects.

Long-term success - Success over a 10-to-20 year period would be reflected in notable profits for investors and the University, establishment of a local biomedical technology industry, and returns from at least one commercial winner sufficient to fund some basic research in addition to sustaining project co-funding. A continuing relationship between UTHSCD and DBC, and possibly with competitive emulators of DBC, could be anticipated.

Consequences of Success - Success of DBC is not without risk to the University. Should DBC be lucky enough to produce one or two really big commercial winners, DBC itself as well as emulators might wish to provide UTHSCD with more commercial sponsorship than required to fill the legitimate funding gap. Although such a problem should be self-correcting in the long run, since extravagant development funding should yield poor returns for investors, in the short run it could distort the appropriate preponderance of basic versus applied research funding in the University setting. Although the University is free to reject funding proposals that threaten this balance, whether it would do so is uncertain.

Failure - Investor satisfaction with DBC is required for the corporation to survive beyond its first five years of operation. This does not mean that DBC must yield profits by then, but it does mean that exciting projects must be progressing toward predictable returns. Otherwise, DBC will dissolve, its capital will return to the investors, and UTHSCD must again rely, at least temporarily, on conventional technology transfer mechanisms.

Consequences of Failure - If this experiment succeeds, no one will care if the credit belongs more to the quality of the University's research or more to the business acumen of DBC. On the other hand, failure might well damage the respect and prestige the University enjoys in the Dallas community. By embarking on this venture, UTHSCD has exposed itself for the first time to community judgment according to business rather than academic standards. This is the principal risk assumed by the University.

Conclusion

The Dallas Mayor's Biotechnology Task Force and UTHSCD have structured DBC to exploit and help manage the commercial opportunities arising from a mature biomedical institution that spends more than $50 million per year on basic research. DBC has also been designed to minimize the consequences of failure, in that investors will not lose their capital and the University is free to use other commercialization vehicles. As a result, failure of DBC need not discourage the University and the Dallas business community from embarking on new experiments in technology transfer that might benefit from experience gained in the present venture.

These precautions notwithstanding, UTHSCD, the DBC investors, and the Hartford Foundation believe Dallas Biomedical Corporation has an excellent chance of meeting all the established criteria for its success, namely:

(1) generation of economic return for its investors,

(2) creation of new investment opportunities for its stockholders,

(3) diversification of the Dallas economy,

(4) translation of research results into public benefit,

(5) retention of creative faculty scientists in the University,

(6) addition of income to the University, and

(7) recognition as a model program of technology transfer.

Thank you for the opportunity to provide this testimony.

DISCUSSION

Mr. WALGREN. Thank you very much, Dr. Neaves. Would you like to comment on just any observations you might make on why venture capital did not come into these areas and fill this gap?

Dr. NEAVES. I believe it is a consequence of the perceived risk that would be entailed by a dedicated corporation in a specific industry coming into a project sooner than its commercial potential has clearly been demonstrated. I do, however, believe that this funding gap should be filled by industrial funding sources and by investor funding sources rather than funds from the Federal Government. The role we believe the Federal Government has in this process is to continue to maintain a strong foundation in basic research that would feed this kind of enterprise.

Mr. WALGREN. But that is not happening even though you believe it should happen. It is not happening, and is this investor-based resource filling this gap to the point where you have falling back on essentially a charitable grant that is being fed out over a period of time in a way that makes the investor capital that you have brought to bear absolutely secure?

Dr. NEAVES. We did not know that we would receive the Hartford grant until the trustees met to make the final decision in the face of the competitive proposals that were before them last December. Dallas Biomedical Corp. was created, and most of the financing was in place before that decision was made. In other words, we had convinced the Dallas business community to go this route with or without the grant from the Hartford Foundation. The

Hartford Foundation stimulated the shaping of this proposal, but the business community's enthusiasm for the concept was such that they were willing to proceed with or without a charitable grant.

Mr. **WALGREN.** But did they agree on $600,000 a year?

Dr. **NEAVES.** We believe we could have raised more capital from the Dallas community. The limit on $12 million was tailored to fit the need as we recognized it in the university without unbalancing the situation. I might add that we do believe that if this experiment is successful, it will demonstrate that profit can be made at an earlier stage of technology transfer than has routinely been perceived by established corporations.

Mr. **WALGREN.** I see.

Mr. Packard.

Mr. **PACKARD.** Thank you, Mr. Chairman, it is not a novel, but certainly an interesting idea. It focuses more on the business rather than academic application. In other words, we have been talking for some time about applied research lagging behind in this country. This is a good example of a sincere effort of trying to bring the business world into producing products from our research, but if it fails, it might set that process back in this country quite some time.

You emphasized, Dr. Neaves, that that success over 10 to 20 years would be reflected in notable profits to the investors and the university, and this one would be lucky if one or two big successful companies would result from it. What assurance do you have that those big one or two successful ventures would locate and return back to the Dallas area its investment into the concept? What is to prevent them, or is there any safeguard to keep those spinoffs from going elsewhere?

Dr. **NEAVES.** There is no constraint in that regard whatsoever, apart from the fact that we believe there is some advantage to companies locating near the source of the intellectual resources that fuel them. That is borne out by the experience of the Stanford-Palo Alto area, and in the Boston area. There are no constraints whatsoever, but we expect that there would be an incentive to remain near the source of innovations that are fueling that company.

Mr. **PACKARD.** Thank you.

Mr. **WALGREN.** Mr. Brown.

Dr. Neaves, you have obviously identified a major gap here, which I am sure you recognize exists in other sectors rather than just the health sector. There is a problem with regard to converting basic research into social benefits. Your model could be an interesting model for some of the other areas. Was that thought of?

Dr. **NEAVES.** That certainly is an interest that has motivated the Hartford Foundation participation. Although their primary focus is on the translation of medical innovation into public benefit, it is, of course, their hope that if successful, what they have participated in creating might well be a model for other realms of science as well.

Mr. **BROWN.** The unique aspect of the institution you have created is that it is a risk-free venture-capital enterprise in the sense that no investor has risks in looking at his investment. That is unusual for venture-capital enterprises.

Dr. NEAVES. We were motivated to structure it in that form because we wanted to minimize the negative impact, in our local community, of failure. In other words, we were extremely concerned about what I characterized as the principal risk that the university entails here. If we don't, as a result of our faith in our own research, cause anyone to make any money here, we at least don't want to embitter potential friends in the Dallas community by telling them that they have no more investment left after 5 years. The tradeoff with that is reduced leverage for their investment. We think that is somewhat counterbalanced by the leverage that they are playing off in the university with its large basic research enterprise.

Mr. BROWN. Well, obviously the proof of the pudding will be the results.

Dr. NEAVES. Yes.

Mr. BROWN. I very much appreciate your presenting this to us this morning.

Thank you, Mr. Chairman.

Mr. WALGREN. Thank you for very much for participating. We might follow up and see in some later exploration, and in letter form, whether there are any other models that you consider when you put this one together, and the pluses and minuses of those, because it certainly makes a lot of sense to have some organized technology transfer mechanism attached to any center of large-scale basic research. So, you are pioneering in a pretty interesting area there. We would like to follow up with you.

Dr. NEAVES. Thank you.

[Questions and answers for the record follow:]

The University of Texas
Health Science Center
at Dallas

Southwestern Graduate School of Biomedical Sciences

William B. Neaves, Ph.D.
Dean

RECEIVED
AUG 13 1986
COMMITTEE ON SCIENCE
AND TECHNOLOGY

August 1, 1986

The Honorable Don Fuqua, Chairman
U.S. House of Representatives
Committee on Science and Technology
Suite 2321 Rayburn House Office Building
Washington, DC 20515

Dear Congressman Fuqua:

Thank you for your letter of 16 July, 1986. Enclosed are the responses to the questions asked by the Members of the Science Policy Task Force. If I can be of further assistance to you, please do not hesitate to call on me at anytime.

Sincerely,

Bill Neaves
William B. Neaves

Enclosure
WBN/bg

5323 Harry Hines Blvd. Dallas, Texas 75235-9004 (214) 688-2509

Follow-up Questions
for
Dr. William Neaves

1. Investigator - initiated basic research is usually based on individual curiosity and not geared to the eventual development of products. Is there a danger in the university-industry biomedical research enterprise that, as financial incentives and pressures increase to perform research with a product objective, the individual desire for knowledge for its own sake could be jeopardized?

2. You indicated the need for development funding to assure technology transfer in biomedicine. In you view, should the Federal Government emulate most other foreign governments by providing more of a mix in basic and applied or development funding? If so, what should the mix be and, what would be the long-term consequences?

3. What means do you use to alert individuals of the potential development opportunities in biomedicine at Southwestern?

4. In your view, should the Small Business Innovative Research program be expanded to meet development funding in the biomedical area?

August 1, 1986

1. This danger only becomes a serious threat to the generation of new knowledge when the funds available for investigator-initiated basic research diminish to the point that productive scientists cannot foresee reliable support for untargeted biomedical research. As long as funding for basic research is adequate, the availability of funds for product development complements rather than competes with the quest for new knowledge for its own sake.

2. The Federal Government should not emulate foreign governments by providing more of a mix of basic and applied (development) funding. Instead, the Federal Government should concentrate its resources in the support of investigator-initiated basic research. It is from this source of new knowledge that product ideas will spring. When they do emerge, funding for their development should come from industry rather than government. An important purpose of the Hartford Foundation grant to the University of Texas Health Science Center at Dallas is to demonstrate to the private sector that investments in early-stage development of product ideas coming from basic biomedical research can be profitable. It is our belief that the potential profitability of new biomedical products will ensure adequate future funding of product development from commercial sources.

3. Until the advent of Dallas Biomedical Corporation, the University of Texas Health Science Center at Dallas had no effective means of informing individuals of potential development opportunities at our institution other than fortuitous contacts between individual scientists and representatives of industry. The professional staff of Dallas Biomedical Corporation, with their network of contacts in the biomedical products industry, now assists the university in publicizing development opportunities.

4. The Small Business Innovative Research program should be broad enough to encompass development funding in the biomedical area. However, the program need not be restructured to give preference to this area.

Mr. **Brown**. Let's turn to Dr. Brown, the director of the Department of Embryology at the Carnegie Institution of Washington.

Dr. Brown, welcome. Please accept our apologies for the time slipping away from us. Feel free to emphasize those points that you would like to make.

[A biographical sketch of Dr. Brown follows:]

DR. DONALD D. BROWN, DIRECTOR, DEPARTMENT OF EMBRYOLOGY, CARNEGIE INSTITUTION OF WASHINGTON, BALTIMORE, MD

Born. December 30, 1931, Cincinnati, Ohio.

Education. Pre-med major, Dartmouth College (3 years, no degree), 1949-1952; M.D. and M.S. in Biochemistry, University of Chicago Medical School, 1952-1956; Passed State Medical Board Examination of Ohio, 1956.

Professional history. Intern, Charity Hospital, New Orleans, 1956-1957; Research Associate and S.A. Surgeon, Public Health Service, National Institute of Mental Health, Bethesda, Maryland, 1957-1959; Special Fellow, National Cancer Institute in the Service de Biochimie Cellulaire, Institut Pasteur, Paris, France, 1959-1960; Special Fellow, National Cancer Institute, Carnegie Institution of Washington, Department of Embryology, Baltimore, Maryland, 1960-1961; Fellow of the Carnegie Institution of Washington, Department of Embryology, Baltimore, Maryland, 1961-1962; Staff Member, Carnegie Institution of Washington, Department of Embryology, Baltimore, Maryland, 1962-1976; Professor of Biology (part-time), Johns Hopkins University, 1969-present; Director, Carnegie Institution of Washington, Department of Embryology, 1976-present.

Organizations. American Society of Biological Chemists; Society for Developmental Biology (Treasurer, 1967-69, President, 1974-75); American Society of Cell Biology (Council, 1971-73); Fellow, American Academy of Arts and Sciences; Member, National Academy of Sciences; Fellow, American Association for the Advancement of Science; Member, American Philosophical Society; President, Life Sciences Research Foundation, 1981- .

Editorial boards. Developmental Biology (1967-70); *Journal of Cell Biology* (1969-72); *Journal of Biological Chemistry* (1971-75); *Journal of Experimental Zoology* (1972-76); *Cell* (1974-77).

Advisory committees. Department of Biology, Massachusetts Institute of Technology (1971-77); Department of Biology, Brookhaven National Laboratory, (1971-75); Department of Biochemistry and Molecular Biology, Harvard University (1976-83); Department of Biology, Harvard University (1978-83); Roche Institute of Molecular Biology (1976-82); CNRS—Gif sur Yvette (1977-); Department of Biochemistry, Princeton University, (1981-1985); Fox Chase Institute for Cancer Research, (1983-); Fred Hutchinson Institute for Cancer Research, (1983-); Department of Molecular Biology, Massachusetts General Hospital, (1983-1985); Whitehead Institute at the Massachusetts Institute of Technology, (1984-); Medical Advisory Board, Howard Hughes Medical Institute (1985-).

Honors. State of Maryland, Young Scientist of the Year, 1966; U.S. Steel Foundation Award in Molecular Biology, 1973; V.D. Mattia Award, Roche Institute for Molecular Biology, 1975; Hon. D. Sci., University of Chicago, 1976; Distinguished Service Award, The Medical Alumni Association, The University of Chicago, 1976; Boris Pregel Award for Biology, New York Academy of Science, 1977; Ross G. Harrison—ISDB Prize in Developmental Biology, 1981; Ernst W. Bertner Memorial Award, University of Texas Cancer Center, 1982; Hon. D. Sci., University of Maryland, Baltimore County, 1983; Rosenstiel Award in Basic Biomedical Science, Brandeis University, 1985; Louisa Gross Horwitz award, Columbia University, 1985.

STATEMENT OF DR. DONALD D. BROWN. DIRECTOR, DEPARTMENT OF EMBRYOLOGY, CARNEGIE INSTITUTION OF WASHINGTON, BALTIMORE, MD

Dr. **Brown**. Thank you, Mr. Chairman, members of the committee. It is certainly a pleasure to testify on behalf of basic research at a time when its relevance cannot be questioned. This biotechnology, which I referred to, is an entirely whole new subsidiary of nonprofit institutions, academic and research institutions. None of this research originated in industry, yet today there is not a major corporation in the pharmaceutical, chemical, food, or energy field that is not investing heavily in biotechnology.

The return for the biomedical research investment has been documented, and in fact, I have taken the liberty of appending a bibliography at the end of my testimony of some articles which do this. They point out two things: one is the cost-effectiveness of biomedical research, and the other is the remarkably circuitous route for discovery from unsuspected and from totally unimagined sources, how these things come together make some innovative discoveries.

Now, I have been asked to give you my thoughts about this remarkable success story, which, of course, has been sponsored by the Congress and the Federal Government in the form of the National Institutes of Health and the National Science Foundation; why this success happened in the United States, which is certainly preeminent in biomedical research.

Following World War II, with Congress' support of the National Institutes of Health, this country became the world center of biomedical research, a place where foreign students must study, do study. It is the center clearly of biomedical research in the world. This is the secret of success of the U.S. biomedical research. It really comes from two policies which are considered to be the National Institutes of Health mode of support. One is the individual-initiated grant system; in the lingo, the RO-1 grants. This is contrasted with the traditional European method of institutional support, where money is given to an institution, leaving the decisions up to senior scientists, chairmen, deans, and university presidents. The National Institutes of Health by contrast, selects directly the individual scientists and awards them by peer review. But the simple difference between individual and institutional research support has enormous significance for every aspect of research. The individual-initiated granting system encourages and rewards individual creativity. It frees young scientists from domination by senior scientists, department heads, deans, and committees who may have very rigid and outmoded ideas about what research projects should be studied. It encourages young scientists to be independent as soon as they can at a time when they are most productive and creative. The European tradition makes young scientists subservient to old scientists. By the time scientists become master of their own fate, more than likely their creative period is over and they are as rigid as their predecessor.

The mechanism for choosing who should be funded for basic research has been well established by National Institutes of Health. It is respected by the scientific community and the envy of scientists throughout the world who are saddled with the European tradition of funding. The selection rules are surprisingly simple. Support the most creative and productive scientists. Beware of limiting scientists either by age, specific subject matter, or geographical location. Since they are chosen for support because they have their own good ideas, no committee is needed to tell them what to study. Research is like professional sports. Scientists are usually most creative, and productive when they are young. As they become older, scientists leave the bench and become chairmen, deans and university presidents. Special attention must be directed to young scientists.

The time-honored peer review system, the integral part of National Institutes of Health's system, works remarkably well as a selection device. Nonscientists are suspicious of peer review where scientists judge each others grant application, accept or reject each others scientific papers for journal publication, and are asked to advise on each others promotions at universities. It sounds like an old boy network, but it isn't. There is such respect for fairness through the merit system amongst scientists that they spend long hours, usually without pay, scrutinizing and judging their colleagues' research.

Stability results when scientists perceive that their science will be judged fairly on merit, and there will be adequate funds to pay for the best science. Stability is designed for the best scientists but not the weaker ones.

The basic research enterprise has three parts that need attention and stability. First, the individual grant system should support the research of an established number of scientists with periodic 5-year reviews. Second, funding of graduate students and postdoctoral fellows must be kept at a certain level as an investment in the next generation of science researchers and teachers. The number of competitive postdoctoral fellowships awarded by the National Institutes of Health was 1,845 in 1978; it has dropped each year to 928 in 1985. Support of trainees is absolutely essential to the research enterprise and, in my opinion, is the most cost-effective item in the research budget. Reduce the level too far and the whole system will topple. Graduate students are one category of personnel who should be supported through institutional grants; postdoctoral fellows, who already have a track record in research, should compete for fellowships just like senior scientists do, on the basis of merit. Third, attention must be paid to physical needs of research—equipment and construction. These grants can also be made on a competitive basis.

The National Academy of Sciences and other organizations have committees that regularly study manpower needs to determine the appropriate number of scientists, graduate students and postdoctoral fellows to maintain vitality in each area of science. These are informed guidelines for establishing the manpower level. See, for example, the 1985 edition of "Personnel Needs and Training for Biomedical and Behavioral Research," published by the Institute of Medicine and the National Academy of Sciences. Granting agencies should assess periodically the equipment and facility needs of grantees and set aside funds for these requirements.

I have been asked to provide this committee with constructive, hopefully even innovative, suggestions in the management of biomedical research. Two current jobs of mine might be of interest to the committee. First, I am the director of a small nonprofit biomedical research department in Baltimore called the Department of Embryology of the Carnegie Institution of Washington, where I am also a bench scientist. The research in our department is concerned with a field called developmental biology. This is a broad area encompassing questions such as how genes control the development of an embryo. How do cells join with each other to form tissues? How is information stored in an egg for later development? The closest applied medical arm of development biology is birth defects. In our department we assume that studying normal embryonic development will periodically give insights into abnormal growth and development of human embryos. Our eight faculty members study a veritable menagerie, including insects, frogs, corn, worms, rats, rabbits, mice, yeast, viruses, and bacteria—literally any creature from which we can extract an answer to some fundamental question of nature. Accordingly, the relevance of our research extends far beyond its application to human birth defects. Our discoveries have contributed to innovations that were completely unanticipated. Part of the beauty and power of nontargeted basic research are unexpected dividends.

As director, I am responsible for our scientific excellence. These are some of the guidelines that I follow. We hire scientists who have personal drive and vision to conceive of and study some original research problem. I care less about the project of the scientists than his or her originality and enthusiasm for science. We reserve considerable laboratory space and resources for young scientists of unusual promise to strike out on their own independent research. We provide scientists with one set of skills, the opportunity to attack very different problems should they choose. If I am a successful director, it is because I look after the inevitable bureaucratic trivia associated with our department. By doing so, I remove nonscientific distractions. Scientific conversations, interactions and advice flow easily among us, but never would I manage or interfere with my colleague's research, only their nonscientific obstacles. The evidence that this strategy works comes from international recognition of our research, including awards to several of our faculty.

My second responsibility, my avocation, is administering a nonprofit foundation called the Life Sciences Research Foundation. Our goal is to convince industry and private foundations to give money with no strings attached for truly nontarget basic research in universities and research institutions. We administer a postdoctoral fellowship program for companies and foundations. Applicants for postdoctoral fellowships from all areas of the life sciences apply to and are screened by our Peer Review Committee of academic scientists. This committee selects finalists on the basis of merit and assigns fellows to industrial and foundation sponsors. It is an arranged marriage between the sponsor and the fellow—neither has a say in the assignment—but the relationship is then nurtured by periodic meetings without obligation. These conditions are designed to eliminate, or at least reduce, the kinds of targeting and restrictions that nongovernmental sponsors are inclined to impose on academic institutions, while still giving these sponsors as many rewards as possible for their largess. It is a way for industry to invest in academia without perturbing the basic research enterprise that works so well. Through these brilliant young scientists whom they sponsor, the industry can keep abreast of the latest experiments being conducted in academic institutions, an interaction that can only enhance intellectual and technology transfer.

So in the two situations where my influence on the research of others has mattered, I have been guided by none other than the National Institutes of Health mode of operation. I have even tried to convince industry and private foundations to use peer review and individual granting methods. I have not been able to improve upon those basic policies.

[The prepared statement of Dr. Brown follows:]

BASIC BIOMEDICAL RESEARCH: A HUGE RETURN ON A FEDERAL INVESTMENT

Donald D. Brown, M.D., Director
Department of Embryology
Carnegie Institution of Washington
115 W. University Parkway
Baltimore, MD 21210

Testimony before the Committee on Science and Technology,
U.S. House of Representatives

April 24, 1986

It's a special pleasure to testify on behalf of basic research at a time when its relevance cannot be questioned. The latest much heralded dividend from basic biomedical research is called "biotechnology". Biotechnology depends upon fundamental discoveries made in such fields as genetics, biochemistry, molecular biology and immunology to name a few. These new methods and ideas are expected to solve just about any problem previously reserved for chemicals. They provide a new approach to understand disease processes, diagnosing disease, and treatment. Agricultural research has high hopes for biotechnology.

Biotechnology was created, developed by, and is wholly the product of basic, nontargeted biomedical research carried out in universities and nonprofit research institutions. Most of the key discoveries were made in the United States which for the past forty years has been preeminent in basic biomedical research. Congress should be proud that this national research enterprise has been supported almost entirely by two enlightened federal agencies, the National Institutes of Health and the National Science Foundation, in proportion to their respective financial commitments to basic biomedical research. None of this research originated in industry. Yet, today there is not a major company in the pharmaceutical, chemical, food or energy field that is not investing in biotechnology.

There cannot be another area of federal support where the return for the dollar is greater. Anticipated profits from biotechnology alone by the end of this century are expected to dwarf all of the accumulated investment the government has ever made in biomedical science. But the government's investment in biomedical research has already been repaid many times. Some industries base their profits on discoveries from biomedical research. The cost of diseases now prevented or controlled because of research exceeds the cost of the original research by an order of magnitude. Research expenses end with the solution of a problem but the benefits from a discovery recur each year that we are rid of that problem. I append to my testimony a bibliography that documents the dollar value to society of fundamental research. Some of these articles trace the torturous and unpredicted path leading from seemingly unrelated discoveries to some useful application.

I have been asked to give you my thoughts about this success story - why it happened in the United States, and something about the procedures, often called the "NIH mode" of supporting research, that account for this success.

The United States became the world's center for biomedical research and training after World War II with Congress' support of the National Institutes of Health. Foreign students are almost obligated to study in the U.S. as a prerequisite for getting a good job in their home country. The secret of success of U.S. biomedical research and what foreign students find so attractive here is NIH's unique and original way of supporting fundamental research called the individual initiated grant system (the RO-1 grants). This is contrasted with the traditional European method of "institutional" support where money is given to institutions leaving decisions up to senior scientists, chairmen, deans and university presidents. The NIH accepts applications for support directly from each individual scientist. Grants are reviewed by a committee of experts who judge the quality of the scientist and the proposed research project. This simple difference between individual and institutional research support has enormous significance for every aspect of research. The individual initiated granting system encourages and rewards individual creativity. It frees young scientists from domination by senior scientists, department heads, deans and committees who may have very rigid and outmoded ideas about what research projects should be studied. It encourages young scientists to be independent as soon as they can at a time when they are most productive and creative. The "European tradition" makes young scientists subservient to old scientists. By the time scientists become master of their own fate, more than likely their creative period is over and they are as rigid as their predecessor.

Fundamental, nontargeted basic research will never dominate our scientific enterprises either in manpower or financial allocations, because there are strong incentives for team research and development targeted toward some short term goal. We need no reminder of the importance of applied research being directed as it is toward specific societal problems. Industry mainly carries out targeted research. However, what is often not appreciated is the debt that applied science owes to the basic research enterprise as it is practiced in universities, and nonprofit institutions. It is here that fundamental knowledge is acquired, normal life processes explained, and the methods developed that will be used in industry for applied research. This information is published openly for the benefit of all. Equally important, it is the nonprofit academic institutions that train scientists for both fundamental and applied research in academia and industry. Thus, the federal government subsidizes profit-making applied research by its support of nonprofit basic research.

Basic research is fragile because its projects often seem obscure and impractical; it is not unified nor directed toward making a useful product. Only occasionally, such as the case with biotechnology, does its relevance surface dramatically and become widely acknowledged. When this happens, there is the temptation to divert resources into a proven area of success often at the expense of less fashionable kinds of inquiry. Thus even success in one area of basic research can destabilize other areas.

There must be an inviolable level of federal support for basic research. Dollars and manpower allocations for applied targets is expected to rise and fall in relation to each problem's severity but this fluctuation should never be at the expense of basic research which is aimed at the support of quality individuals rather than the solution of specific problems.

The mechanism for choosing who should be funded for basic research has been well established by NIH. It is respected by the scientific community and the envy of scientists throughout the world who are saddled with the European tradition of funding. The selection rules are surprisingly simple. Support the most creative and productive scientists. Beware of limiting scientists either by age, specific subject matter, or geographical location. Since they are chosen for support because they have their own good ideas, no committee is needed to tell them what to study. Research is like professional sports. Scientists are usually most creative, and productive when they are young. As they become older, scientists leave the bench to become chairmen, deans and university presidents. Special attention must be directed to young scientists.

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Universities guarantee tenure to the best members of their science departments but the funding agencies do not and should not guarantee tenure for research support. Scientists must apply periodically to granting agencies. Five years is an appropriate length of time between reviews, perhaps on rare occasions ten years. Five years is long enough for stability but not so long as to inspire complacency. Not the most famous prize winning scientist should be free of periodic reevaluation. The peer review system guarantees the tax payers their money's worth on the one hand and the necessary stability for a scientist on the other. Stability results when scientists perceive that their science will be judged fairly on merit, and there will be adequate funds to pay for the best science. Stability is designed for the best scientists but not the weaker ones.

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My second responsibility, my avocation (pro bono), is administering a nonprofit Foundation called the Life Sciences Research Foundation (LSRF). Our goal is to convince industry and private foundations to give money with no strings attached for truly nontarget basic research in universities and research institutions. We administer a postdoctoral fellowship program for companies and foundations. Applicants for postdoctoral fellowships from all areas of the life sciences apply to and are screened by our Peer Review Committee of academic scientists. This Committee selects finalists on the basis of merit and assigns fellows to industrial and foundation sponsors. It is an arranged marriage between the sponsor and the fellow neither has a say in the assignment - but the relationship is then nurtured by periodic meetings without obligation. These conditions are designed to eliminate, or at least reduce, the kinds of targeting and restrictions that nongovernmental sponsors are inclined to impose on academic institutions, while still giving these sponsors as many rewards as possible for their largess. It is a way for industry to invest in academia without perturbing the basic research enterprise that works so well. Through these brilliant young scientists whom they sponsor, industry can keep abreast of the latest experiments being conducted in academic institutions, an interaction that can only enhance intellectual and technology transfer.

So, in the two situations where my influence on the research of others has mattered, I have been guided by none other than the "NIH-mode" of operation. I have even tried to convince industry and private foundations to use peer review and individual granting methods. I have not been able to improve upon those basic policies.

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DISCUSSION

Mr. **Walgren**. Very interesting. Do we do much of this that you are doing through the foundation? Is that a blip on the horizon of our landscape of American science at this point, or is it that kind of looking for money in the private sector from industry and from other charitable organizations, and giving it to nontargeted basic research? Does that happen very much?

Dr. **Brown**. The blip in terms of total postdoctoral fellow-ship support is really just a blip, not even a notable one. There are, as you can see from the figures, somewhere in the order of a thousand competitive postdoctoral fellowships awarded by National Institutes of Health. We gave away eight. We are talking about a very small project, a very small foundation, attempting to ask major industry to set aside some fraction of their academic support for truly nontargeted research, watering the roots so to speak, for the future.

Mr. **Walgren**. If the National Institutes of Health did a 1,000, eight seems a significant number for one small entity.

Dr. **Brown**. Eight compared to a 1,000? It seems small to me. Eight chosen I might state, out of 400 applicants for this fellowship program. We awarded eight.

Mr. **Walgren**. Does that then mean there are a lot of applicants not finding a support home at this point?

Dr. **Brown**. In this particular group, there are a lot who would not otherwise be funded find it because we opened our doors for applicants who are not otherwise serviced by traditional agencies, such as ecologists, population geneticists, and planning biologists, who by the way, have a terrible time finding support. In that sense, our eight does more good than the number implies.

Mr. **Walgren**. Do they maintain a relationship with your institute for a long time?

Dr. **Brown**. It is a 3-year postdoctoral fellowship. Each year they must agree to visit the company to increase the interaction with the company that we assigned them to. The company has no say in the scientific area of the fellow. As you can see, this decreases their enthusiasm in our program, but our argument is that industry should set aside a fraction of their money for this kind of broad-range, wide-net support. That is where the recombinant DNA of 10 years from now is likely to come from.

Mr. **Walgren**. It is the stability in the scientists that are involved in the university aspect. Are those people that you chose, do you find them staying with you and are they—I guess what I am trying to get at, you are making an initial selection of enthusiastic interested original people—does that remain?

Dr. **Brown**. You must realize that that is still their training period—the postdoctoral period of 3 years, after which they begin a job usually in academic institutions. The program is only in its fourth year, so it is a little bit too early to tell you now. I can say that the fellows that have graduated from it have gotten very distinguished jobs indeed. So we chose well.

Mr. **Walgren**. Mr. Brown.

Mr. **Brown**. Dr. Brown, you have put great emphasis upon the creative mind and other witnesses have—Dr. Berg was very emphatic on this also. I am interested—I hope the Congress will be interested—in looking at this from the most fundamental level. You have contrasted the institution arrangement, the National Institutes of Health model, with the European model and we look at it in terms of how much tax money shall we invest in it, so I really tend to think these are somewhat superficial analyses of the thing, and I will explain why I say this.

Our science in this country has actually burgeoned, blossomed, on just, to some degree at least, on just the immigrant European scientists who would be trained under this system that you didn't speak so highly of, our great progress in agricultural science, and productivity came out of the same kind of system. It can't be just a system that is flawed or that is imperfect.

If we are exaggerating a little bit for the National Institutes of Health, there has to be some other element involved here. I am trying to understand what that element is. It can't be just money, because there seems to be almost a rule of thumb if you have so much money you get three or four times as many people applying as there is money available. No matter what amount of money, that ratio remains fairly constant.

What limits are there on the supply of critical, analytical, imaginative, problem-solving people? Are there any limits? Is the whole population capable of doing this? What elements in these two systems are really critical, not just whether it is a formula funding versus an individual or grant funding? What elements are essential? Have you thought about it a little bit?

Dr. BROWN. I would like to return to your earlier point you made about Europeans coming to this country. It is here where they did their successful research really, and the climate was extremely unfavorable for them there.

Mr. BROWN. There are a few exceptions—Einstein and others—go ahead.

Dr. BROWN. Of course there are exceptions. But what you want me to do is to somehow give you a formula for what number of people needs to be supported or how one ever gets to the end of this. You visualize the scientist sort of questing for continual increases. Well, there are, of course, studies on what the basic level should be of biomedical personnel at all levels, and I have made a mention in my testimony of where that can be found. The National Academy of Sciences makes these every year, I believe, and the Institute of Medicine.

I frankly am not one who believes that the scientific enterprise must continually expand. In fact, the number of new grants at National Institutes of Health is not any more now than it was 5 or 10 years ago.

Mr. BROWN. I will agree with you, we don't have enough. I am not looking at this from an OMB standpoint, I am looking at it from the standpoint of really what is in the national interest, and how we can motivate the Nation and its elected leaders to recognize we want to reach that level that is in the national interest.

Dr. BROWN. I am interested to know what argument you feel is the most creative one. Is it the amount of dollars returned on the dollar invested? Because in that case, it is extremely effective.

Mr. **Brown**. In my mind the fundamental—of course, I don't think many Congressmen share this—is the degree to which we can productively use human resources for the enhancement of human knowledge, and there is only a certain number of people who are motivated to even seek the answer.

Dr. **Brown**. That is why I think this biomedical system is so extremely good, because it is selective. It is selective on the basis of creativity and productivity by virtue of continual competition, which is competition on the basis of hiring originally by first-class schools that support for this research which are not infinite in number. Then no tenure is ever involved in the awarding of research support to the National Institutes of Health/NSF system. That is, even the most distinguished scientists must reapply periodically to their peers, and be reevaluated and believe me, they do get turned down.

Mr. **Brown**. Let me be cross, Doctor. This great institutional system of ours turns out 1,000 or 2,000 postdoctoral research fellows every year; that is about what we support. There are 15,000 or 20,000 who go into the practice of medicine because rewards are so much greater. There is no indication, in my mind, that there are any less intelligence or problem solving or anything else, than the others. Maybe there is evidence that I am not aware of. It seems to me it is strictly a money-driven proposition. They are not all saints who are merely seeking to save human lives.

Dr. **Brown**. These bright postdoctoral fellows, who come to our laboratory and whom we depend on to do research are very enthusiastic and work all hours. With regard to these people, they are not financially driven people.

Mr. **Brown**. I am not saying these, these ones who are not, I am saying there are 10 times as many who go into something that is more lucrative, more financially rewarding, and they can't all be incapable of doing brilliant research, they just don't choose to do that.

Dr. **Brown**. There are a lot of extremely brilliant people who simply don't have the motivation or interest in doing bench science. There are many of these that don't have quite the same skills and ability to do this kind of work, but have a high ability to understand language skills and even mathematical skills. Those are not necessarily the skills which make for a first-class bench scientist in a wet lab. They are not predictably related. I think it is required but it is not sufficient.

Mr. **Brown**. All of your great national intelligence testing organizations would assure you that those tests do indicate who the most intelligent, capable people are.

Dr. **Brown**. Not the best scientists. I won't go for that in a moment.

Mr. **Brown**. Thank you very much.

Mr. **Walgren**. Well, thank you very much, Dr. Brown, we appreciate it.

[Questions and answers for the record follow:]

SCIENCE POLICY TASK FORCE

Hearings on Policies for Biomedical Research

April 24, 1986

Followup Questions for Dr. Donald D. Brown

1. **It has been reported that the burden associated with requests for research funding support and other administrative duties may (1) influence the choice of research projects by investigators and institutions and, (2) take needed time away from doing research. To what extent is this true in the biomedical sciences? If there is a trend, will it continue in the long term? What actions by the Government and scientific community could remedy this situation?**

   The current National Institutes of Health granting procedure is excellent. Every five years a scientist must reapply for support on the basis of progress during the preceeding five years. Shorter periods of support are not realistic and demand too much paper work. Longer pericds result in extended and unwarranted support of weak scientists. To my knowledge, only the NIH awards five-year grants.

2. **You stress the importance of supporting and muturing young scientists as one of the most important investments we can make for the future progress of biomedical research. The initiatives of the Life Sciences Research Foundation is a step in this direction.**

   Since there is an increasing demand for trained scientists by both industry and academia, can you suggest a more definitive program whereby industry provides a fair share of support for training young researchers at universities?

   One of the reasons that we established the Life Sciences Research Foundation was our recognition of the importance of training for research in academia and in industry. LSRF is run out of my office with no full time paid help. We estimate that we could only administer about 100 3-year post doctoral fellowships using our present structure. It would be very simple to organize a cost effective administrative unit to administer 5000 such fellowships. The real problem is to convince industry to share the costs. Sometimes it has taken me four years of solicitation, letters from others and cajoling to convince a large, research oriented company to support just a single fellow. This, despite the tax advantages to industry which subsidize more than half their cost of each fellowship. We estimate that each $30,000 fellowship costs the sponsor just $13,000 if they made use of both tax deduction and the research tax credit available under the legislation passed several years ago.

   The German Chemical Industry has banded together to help academia by pledging a certain small percentage of their profit to be held by a nonprofit agency (perhaps like LSRF). This is then parceled out to the various universities in Germany by a prearranged formula. I prefer a variant of this idea that is more in tune with the U.S. system of rewarding individuals rather than institutions. Thus, U.S. companies who benefit from research in nonprofit institutions would pledge a certain percentage of their profits for the purpose of training young scientists. A nonprofit organization such as LSRF would review all candidates, and award fellowships to the very best scientists. Fellows would be assigned to companies to ensure close interaction between sponsor and awardee. Of course fellows would only work in nonprofit institutions. This is basically how LSRF works, but we do so on a very small scale.

3. **Since most young researchers go through post-doctoral training, do you find that their ability to compete for funding support is based more on who they trained with rather than their capabilities?**

It is true that scientific "linkage" matters at the start of a career. A weak scientist trained in a famous laboratory would have a better chance at a job than his/her counterpart trained in the laboratory of a less well known scientist. However this slight advantage disappears very quickly as the young scientist is expected to make his/her own mark. The same is true for funding competition.

4. **You indicated that a significant number of foreign investigators are being trained in our tax-supported universities.**

Since many of these scientists return to their native countries, are we contributing to a "brain drain" by indirectly supporting foreign research enterprises and by partially supporting them to be our economic competitors?

In a sense this is true. To my mind the most extreme example is the Japanese. The Japanese tradition has never recognized the need for advanced training so they give very few fellowships. However, all young graduates recognize the importance of postdoctoral training and the advantages for their future employment if they train for several years in the U.S. In the field of biomedical research, there are hundreds of young Japanese postdoctoral fellows in U.S. institutions each year, and the U.S. pays the entire bill (i.e., salary, travel, research expenses). Last year I visited Japan and confronted business leaders with this paradox. They admitted it but felt powerless to change things. I then wrote a letter to Prime Minister Nakasone suggesting that one (albeit it small) way to reverse the balance of payments between our countries was for the Japanese government to set up a postdoctoral fellowship program which would pay for their many young scientists who go abroad for training. I have not yet heard from him. Some Japanese scientists elect top stay in the U.S. because of the better job market for biomedical researchers and because of our enlightened granting policies. So it is true that we are training foreign scientists who will be leaders in foreign efforts that compete with us, but we are also employing many of them in our own companies.

5. **The need top maintain up-to-date laboratories and equipment for support of present sophisticated biomedical research needs attention not only at large, prestigious universities but also at smaller, lesser known schools.**

How can all these institutions be equally competitive for the funds available?

One of the features of biomedical research in this country of which I most approve has been the large number of universities and research institutions that have contributed to the many great scientific advances of the past forty years. The individual granting system is supplemented with special equipment grants. These are also reviewed on the basis of need and quality. Regrettably there are no Federal funds for construction which in a sense gives some weaker schools who might not compete well something of an advantage. For example, public institutions who can rely on State support and any private institution with strong alumni support have independent means to raise money for buildings and facilities. Inevitably, needy but deserving institutions "fall between the cracks" just like some individual researchers, when forced to compete for limited funds. However, I believe that there must be critical review for both equipment and construction grants. There is no substitute for quality as a criterion for Federal grant support.

Mr. **Walgren.** Dr. Mac Lachlan, welcome to our process and please proceed as you would like.

[A biographical sketch of Dr. Mac Lachlan follows:]

Dr. Alexander Mac Lachlan

Alexander Mac Lachlan, senior vice president-technology, joined the Du Pont Company in 1957 as research physicist in the Engineering Department. Four years later he was promoted to the position of senior research physicist. In 1962 he was named research associate and the following year he became a supervisor. In 1965 Dr. Mac Lachlan was transferred to the Central Research Division as a supervisor and four years later he assumed the responsibilities of research manager in the Photo Products Department. In June 1974 he became director of research and development, Photo Products-Europe, with Du Pont de Nemours (Deutschland) GmbH. He returned to Wilmington in September 1975 on special assignment in the Photo Products Department and was named director of marketing in the Printing Sales Division, Photo Products Department, in May 1976. In December 1978 he was transferred to the Plastic Products and Resins Department as director for "Nafion" products, Plastic Products Division. He became director of the Research and Development Division of the Chemicals and Pigments Department in September 1980. He was appointed assistant director of the Central Research and Development Department in March 1982 and named director of that department in October 1983. He was promoted to his present position in January 1986.

Born Jan. 22, 1933, in Boston, Mass., he was graduated from Tufts College in 1954 with a Bachelor of Science degree in chemistry. Three years later he received a doctorate in physical organic chemistry from the Massachusetts Institute of Technology.

Numerous articles by Dr. Mac Lachlan have been published in technical journals. He also holds several patents.

He and the former Elizabeth E. Pegues of Shreveport, La., were married in 1958. They have four children, Katherine, Amy, Mary, and Alexander. The family lives at 1501 Turkey Run Road, Wilmington.

STATEMENT OF DR. ALEXANDER Mac LACHLAN, SENIOR VICE PRESIDENT-TECHNOLOGY, E.I. DU PONT DE NEMOURS & CO., INC., WILMINGTON, DE

Dr. **Mac Lachlan.** Thank you very much, Mr. Chairman, and members of the committee. I will not follow my supplied remarks exactly, I will do it in the same order that they are submitted, but I will try to compress and paraphrase as I go along.

In 1986, our company will spend over $1 billion on research and development, of which some $200 million is committed to the health sciences—more than twice our 1981 expenditure in this area. Our expanded effort in health care research is also reflected in our basic research programs in biotechnology, where we are now spending about $50 million annually—over three times our 1981 expenditure.

Biotechnology promises to bring us immense health care benefits through new and better therapeutics, such as insulin and human growth hormone; diagnostics, accurately testing for a variety of diseases; and vaccines, perhaps cleaner and safer than ever before. It also brings us instrumentation for new types of therapies, new processes for drug and chemical synthesis, and new methods for the treatment of toxic substances and wastes.

Because of these incentives, we are employing our well-established strengths in the physical sciences, engineering, and manufacturing in a concerted effort to build our presence in biomedical research, with biotechnology as a major area of concentration. Over the past 5 years, we have invested over $150 million in life science-related laboratory facilities. In parallel, we have been building a high quality staff in both basic and applied research. Our basic scientists, numbering over 200, are trained in molecular biology, genetics, immunology, and related disciplines. That expansion in basic research personnel has been paralleled in our operating departments with new staff to support our planned growth in pharmaceuticals, diagnostics, biological research instrumentation, research chemicals, and other health-related areas.

In addition to the significant opportunities, there are also significant management challenges related to the transformation of biotechnological research into useful products.

As our approach to this challenge we selected a principal strategy involving the creation of a substantial in-house capability in modern biology. Our main reasons were threefold. First, we, like many other large corporations worldwide, felt it was critical to build an internal strength to allow us to become familiar with these new technologies. Second, we wished to be able to translate rapidly biotechological advances, from both inside and outside Du Pont, into commercial products. Last, we wanted to be mature enough in our scientific capabilities to be an attractive partner in collaborative ventures, recognizing the importance of the vast amount of research in universities and elsewhere.

Our ultimate goal, and our current direction, is to contribute Du Pont's strengths to collaborative partnerships with the main groups concerned with biotechnological R&D; I am speaking here of our colleagues in academia, large and small business, and Government. As partners, these groups can and must work together in a much larger way than can any single entity. I would like to take the next few minutes to describe how Du Pont has been working with each type of partner to strengthen our future in these emerging new technologies. In mentioning partners, I should also include the public as a whole, because the public must be with us in order for us to advance in these technologies without severe competitive restraints.

One major partner in our efforts has been academia. Over the past several years, we have established numerous relationships with university researchers in order to gain access to their expertise in technology, to help us recruit and train high-quality scientists, and to provide a unique opportunity for our management to receive feedback on the quality and direction of our internal programs. Additionally, these relationships provide our scientists peer contact for sharing ideas, and, last but not least, these relationships provide an early look at scientific developments that can lead to new products.

One example of our involvement with academia is our continuing program of major support for the laboratory of Dr. Philip Leder at Harvard Medical School. Dr. Leder is a renowned authority in the field of molecular genetics, and his laboratory has led the field of research in oncogenes, the genes relate to be vital to the understanding of certain cancers. Several years ago Du Pont funds helped Dr. Leder establish his laboratory at Harvard, and we continue to support a significant amount of his work. We view this as a long-term commitment. To date, in addition to an excellent two-way flow of information and collaboration between Dr. Leder and Du Pont, three of our Ph.D. scientists have spent extensive time in his laboratory, receiving a balanced training in molecular biology research. Several elements of his work are now being incorporated into research at Du Pont, and may someday become useful diagnostic and therapeutic products. Although patent considerations are involved, our agreement does not interfere with publication or with the free exchange of information among students and colleagues.

Another example of major Du Pont support is our recent commitment to the Whitehead Institute for Biomedical Research in Cambridge, MA, representing $4½ million over 5 years. This relationship is in the form of general support and is somewhat less structured than the one with Dr. Leder. However, funding for the Whitehead Institute is designed to give our scientists and management access to outstanding biomedical researchers. We expect to benefit from an early look at their research as well as from our evolving collaborative projects.

In addition to these two arrangements, which are aimed at promoting collaboration with outstanding researchers, there are many other examples of support for academic laboratories relating to projects that give us access to specifically-directed forefront research. One such example is our extracorporeal therapy program, where we are utilizing our engineering and biomedical research skills in collaboration with academic researchers to develop therapies for several diseases. Specifically, there are certain diseases that are accompanied by a buildup of unwanted components in the blood, leading to significant patient distress, and sometimes death. Extracorporeal therapies involve the sterile shunting of blood outside the body, where the unwanted components are filtered out. Biotechological processes allow for the specific identification and removal of these components. Over the last 4 years, Du Pont has given about $1.6 million to universities in support of research directed at employing extracorporeal dialysis to treat diseases such as systemic lupus erythematosus, kidney transplant rejection, Fabry's and Goodpasture's diseases, multiple sclerosis, and others. This melding of Du Pont's internal resources with basic research in academia should allow us to make significant contributions to the treatment of these debilitating diseases. By any measure, this is high-risk research, with the hoped-for payoff many years away.

The second major partner in our efforts to successfully commercialize health-care products is the biotechnology industry. Over the past few years, we have formed relationships of various types with several small biotechnology firms to combine their expertise with ours. Often, they have concentrated their research in areas that become critical to our business direction. To avoid duplicating their work, we have initiated relationships with them to fill in our areas of need. These relationships range in size and type from our purchase of New England Nuclear, with their monoclonal antibody and radiochemical know-how, to agreements with Centocor for the joint development of test systems for AIDS and hepatitis.

To date, we have formed many of these relationships, representing a very large investment. We expect this type of involvement with the biotechnology industry to grow over the next few years as we work to bolster and solidify our in-house research efforts. While Du Pont has had a long history of collaboration to develop commercial successes, I do believe that the extent and number if greater than ever before. We think this is a healthy trend, as it ensures the commercialization of valuable developments in biotechnology.

The third key partner in our efforts to develop biotechnology expertise is the Federal Government. Although the relationship between industry and Government has often been based on advice and regulation, other types of relationships are forming to help commercialize the products of biotechnology. Let me illustrate by describing two we have recently developed because of their potential importance for public health care.

Du Pont has set up a program that supplements and parallels the project of Dr. Steven Rosenberg at the National Cancer Institute, relating to his innovative lymphokine activated killer cell therapy used in the treatment of cancer. This encouraging therapy involves removing cells from the blood of cancer patients, treating the cells outside the body with genetically-engineered Interleukin-2, and then returning the treated cells to the body—all under sterile conditions. However, this is a highly complex and expensive procedure. Du Pont's program includes $5 million in annual spending, and about 15 scientists, to investigate LAK and other extracorporeal therapies, including those previously described. This has become a collaborative effort with Dr. Rosenberg's research team, and in fact, we provided the Interleukin-2 used in his first phase I clinical trial. In addition to the biomedical aspects, many other technologies need to be advanced for the success of this project. Here, the strength and diversity of a company such as Du Pont come into to play. We hope to use our knowledge of separations technology, engineering, and instrumentation to help make extracorporeal therapy for cancer treatment a practical reality. This support of Government research is voluntary, and is based on scientific collaboration rather than contractual agreement. The synergy derived from such a sharing relationship will lead, we hope, to a new form of partnership between Government and industry.

Another example of our successful interaction with Government laboratories is our development of new diagnostic tests for AIDS, in conjunction with work from the laboratory of Dr. Robert Gallo, of the National Cancer Institute. This project also involves our work with Biotech Research Laboratories, a small biotechnology company in which we have an equity stake. Additionally, collaborative research with Dr. Dani Bolognesi of Duke University is an important element of these efforts. As an extension of this research, Du Pont is investigating the possibility of developing vaccines and antiviral agents targeted against AIDS.

Thus, there is a complementary role between the key players—industry, academia, and government—leading to U.S. strength in biotechnology. The public will be the ultimate beneficiary of the new health-care products and the enhanced quality of life that will result. The Government can act as a major partner in our efforts to remain successfully competitive in the innovation and commercialization processes.

Future legislation should be supportive of American biotechnology. For example, to best meet our health-care goals, companies in the United States will often need to work closely together and create novel relationships with each other. Legislation may be required to condone and help foster increased collaboration between companies.

Government programs could also be targeted at communicating the benefits and risks of biotechnology to the public and to State and local officials. Enhanced communication would help people to better understand the health-care benefits of biotechnology, and allow the public to appreciate the regulatory steps taken to protect its safety. Industry and individual scientists should also share in this communication process.

Future support of academic programs should not only be directed at advancing basic research, but should also focus on efforts that relate to the developments of products of biotechnology, such as a cell growth technology and fermentation engineering. Foreign governments have made this a focus of their strategies for biotechnology. Recent National Science Foundation support for a fermentation process center at the Massachusetts Institute of Technology is a good step in this direction.

Of significant concern to us are the liability actions that are presently forcing many health-care practitioners and biomedically-related companies out of the health-care business. The incentive to develop new vaccines, pharmaceuticals, and other related products has been drastically decreased. There is an immediate need for legal reforms that bring fairness, balance, and predictability to the liability system. Such actions would ultimately benefit the public by allowing for new biomedical discoveries and helping to contain the costs of health care.

In sum, our Federal Government can act as a major partner to help bridge the gap between basic research and the ultimate commecialization of biotechnological products. It can help protect the public it serves while still allowing the United States to maintain the leadership position it has established. Government can assist the other key partners—industry and academia—to best make their contributions. Stated otherwise, if American leadership in basic research can be translated into leadership in commercialization and improvement of health care, the result will be a bolstering of the gross national product and increased employment. On the other hand, without Government as a partner assisting that effort, these revenues and jobs may not be realized at a level reflective of U.S. contributions to basic research in modern biology.

[The prepared statement of Dr. Mac Lachlan follows:]

Remarks By

Alexander Mac Lachlan
Senior Vice President - Technology
E. I. du Pont de Nemours & Co., Inc.

Before The
Committee On Science And Technology
Science Policy Task Force
Of The
United States House of Representatives
Washington, DC
April 24, 1986

BIOMEDICAL RESEARCH TESTIMONY--BIOTECHNOLOGY AT DU PONT
HOUSE COMMITTEE ON SCIENCE AND TECHNOLOGY
ALEXANDER MAC LACHLAN
APRIL 24, 1986

Mr. Chairman, Members of the Committee, my name is Alexander Mac Lachlan. I am the Senior Vice President for Technology at the Du Pont Company. In 1986, our company will spend over one billion dollars on research and development, of which some 200 million dollars is committed to the health sciences -- more than twice our 1981 expenditure in this area. Our expanded effort in health care research is also reflected in our basic research programs in biotechnology, where we're now spending about 50 million dollars annually -- over three times our 1981 expenditure. Biotechnology involves the use of living cells to produce commercial products, and employs a number of scientific disciplines including molecular biology, genetics, immunology, and others. Du Pont is allocating its resources in a concerted effort to turn basic biotechnological research into commercially viable products.

Biotechnology promises to bring us immense health care benefits through new and better therapeutics, such as insulin and human growth hormone; diagnostics, accurately testing for a variety of diseases; and vaccines, perhaps cleaner and safer than ever before. It also brings us instrumentation for new types of therapies, new processes for drug and chemical synthesis, and new methods for the treatment of toxic substances and wastes. In addition, large future revenues are predicted to be earned by these products.

Because of these incentives, we are employing our well-established strengths in the physical sciences, engineering, and manufacturing in a concerted effort to build our presence in biomedical research, with biotechnology as a major area of concentration. Over the past five years, we have invested over 150 million dollars in life science-related laboratory facilities. In parallel, we have been building a high quality staff in both basic and applied research. Our basic scientists, now numbering over 200, are trained in molecular biology, genetics, immunology, and related disciplines. This expansion in basic research personnel has been paralleled in our operating departments, with new staff to support our planned growth in pharmaceuticals, diagnostics, biological research instrumentation, research chemicals, and other health-related areas.

In addition to the significant opportunities, there are also significant management challenges related to the transformation of biotechnological research into useful products.

As our approach to this challenge, we selected a principal strategy involving the creation of a substantial in-house capability in modern biology. I have already mentioned that we have built a quality staff of over 200 scientists to perform this research. Our main reasons were threefold: First, we, like many other large corporations worldwide, felt it was critical to build an internal strength to allow us to become familiar with these new technologies. Second, we wished to be able to translate rapidly biotechnological advances, from both inside and outside Du Pont, into commercial products. Last, we wanted to be mature enough in our scientific capabilities to be an attractive partner in collaborative ventures, recognizing the importance of the vast amount of research in universities and elsewhere.

Our ultimate goal, and our current direction, is to contribute Du Pont's strengths to collaborative partnerships with the main groups concerned with biotechnological R and D: I'm speaking here of our colleagues in academia, large and small business, and government. As partners, these groups can and must work together in a much larger way than can any single entity. I would like to take the next few minutes to describe how Du Pont has been working with each type of partner to strengthen our future in these emerging, new technologies. In mentioning partners, I should also include the public as a whole, because the public must be with us in order for us to advance in these technologies without severe competitive restraints.

One major partner in our efforts has been academia. Over the past several years, we have established numerous relationships with university researchers in order to gain access to their expertise in technology, to help us recruit and train high quality scientists, and to provide a unique opportunity for our management to receive feedback on the quality and direction of our internal programs. Additionally, these relationships provide our scientists peer contact for sharing ideas, and, last but not least, these relationships provide an early look at scientific developments that can lead to new products.

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The second major partner in our efforts to successfully commercialize health care products is the biotechnology industry. Over the past few years, we have formed relationships of various types with several small biotechnology firms to combine their expertise with ours. Often, they have concentrated their research in areas that became critical to our business direction. To avoid duplicating their work, we have initiated relationships with them to fill in our areas of need. These relationships range in size and type from our purchase of New England Nuclear, with their monoclonal antibody and radiochemical know-how, to agreements with Centocor for the joint development of test systems for AIDS and hepatitis. As another example, we recently entered an agreement with Cistron Technology to procure access to basic research and production technologies for Interleukin-1, a relationship that will ultimately assist in our ongoing research projects involving arthritis and cancer.

These agreements with biotechnology companies give us immediate access to potential new products and allow us to vertically integrate basic research with our development, production, and marketing strengths. To date, we have formed many of these relationships, representing a very large investment. We expect this type of involvement with the biotechnology industry to grow over the next few years as we work to bolster and solidify our in-house research efforts. While Du Pont has had a long history of collaboration to develop commercial successes, I do believe that the extent and number is greater than ever before. We think this is a healthy trend, as it ensures the commercialization of valuable developments in biotechnology.

The third key partner in our efforts to develop biotechnology expertise is the federal government. Although the relationship between industry and government has often been based on advice and regulation, other types of relationships are forming to help commercialize the products of biotechnology. Let me illustrate by describing two we've recently developed because of their potential importance for public health care.

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Additionally, collaborative research with Dr. Dani Bolognesi of Duke University is an important element of these efforts. As an extension of this research, Du Pont is investigating the possibility of developing vaccines and antiviral agents targeted against AIDS.

Thus, there is a complementary role between the key players -- industry, academia and government -- leading to U.S. strength in biotechnology. The public will be the ultimate beneficiary of the new health care products and the enhanced quality of life that will result.

The government can act as a major partner in our efforts to remain successfully competitive in the innovation and commercialization processes. This is especially important in light of significant foreign competition in biotechnology, most notably from Japan.

Future legislation should be supportive of American biotechnology. For example, to best meet our health care goals, companies in the United States will often need to work closely together and create novel relationships with each other. Legislation may be required to condone and help foster increased collaboration between companies.

Government programs could also be targeted at communicating the benefits and risks of biotechnology to the public and to state and local officials. Enhanced communication would help people to better understand the health care benefits of biotechnology and allow the public to appreciate the regulatory steps taken to protect its safety. Industry and individual scientists should also share in this communication process.

Future support of academic programs should not only be directed at advancing basic research, but should also focus on efforts that relate to the development of products of biotechnology, such as cell growth technology and fermentation engineering. Foreign governments have made this a focus of their strategies for biotechnology. Recent NSF support for a fermentation process center at the Massachusetts Institute of Technology is a good step in this direction. We hope to see increased federal support for similar programs in the future.

Of significant concern to us are the liability actions that are presently forcing many health care practitioners and biomedically-related companies out of the health care business. The incentive to develop new vaccines, pharmaceuticals, and other related products has been drastically decreased. There is an immediate need for legal reforms that bring fairness, balance, and predictability to the liability system. Such actions would ultimately benefit the public by allowing for new biomedical discoveries and helping to control the costs of health care.

In sum, our federal government can act as a major partner to help bridge the gap between basic research and the ultimate commercialization of biotechnological products. It can help protect the public it serves while still allowing the United States to maintain the leadership position it has established. Government can assist the other key partners, industry and academia, to best make their contributions. Stated otherwise, if American leadership in basic research can be translated into leadership in commercialization and improvement of health care, the result will be a bolstering of the Gross National Product and increased employment. On the other hand, without government as a partner assisting that effort, these revenues and jobs may not be realized at a level reflective of U.S. contributions to basic research in modern biology.

For its part, Du Pont is committed to using its vigorous internal R and D program, coupled with its unique strengths in chemistry, materials science, and engineering, to forge ahead in biotechnology, while at the same time reaching out in cooperative ventures with the other stakeholders in these new and exciting sciences.

All of the necessary pieces are at our disposal. We are all partners in, and the mutual beneficiaries of, these new technologies. As partners, we can and will learn how best to fit those pieces together to form a cohesive whole that will encourage scientific inquiry while providing a framework for the development of products that will meet real, human needs for many years to come.

I will be happy to answer any questions.

DISCUSSION

Mr. **Walgren**. Thank you very much, we appreciate that. What is Japan doing in biotechnology at this point?

Dr. **Mac Lachlan**. I think they are really concentrating on the commercialization aspects of it. They are also certainly strengthening their basic research. Japan has a long history in the whole area of fermentation, and all the engineering and other skills that are related to taking a material that is produced biologically to a form that can be used commercially. In the United States, we are certainly bolstering that right now, but I think it is still an area of weakness in this country. Japan has recognized our weakness and is apparently capitalizing on this as an opportunity. It, of course, is also part of their culture to focus on such strategic areas and develop them. They don't do it with a giant amount of money; they do it basically by urging cooperation among various industries. I don't propose that we follow that system, but we should recognize that they are tough competitors.

Mr. **Walgren**. How do you respond to the previous project which tried to fill this demonstration gap, that venture capital does not seem to enter into?

Dr. **Mac Lachlan**. I am sorry, I don't quite follow.

Mr. **Walgren**. I am thinking that there apparently is this failure of venture capital to take basic research and make it——

Dr. **Mac Lachlan**. Yes.

Mr. **Walgren** [continuing]. Available, not available but translated into commercial?

Dr. **Mac Lachlan**. Yes.

Mr. **Walgren**. And your indication here was that you would like to see the National Science Foundation involved in things like the experimentation institute; I guess again staying very much on the basic side, but there apparently is a reluctance of venture capital to fill that gap. In that instance you had a city and a university and a charitable foundation all using essentially nonprofit based resources, putting some resources in to provide some developmental moneys that apparently were not forthcoming otherwise.

Dr. **Mac Lachlan**. I think it is fairly straightforward to see the venture capitalist's problem. They have only so much money that they can raise, and they are basically covering the early stages of development. I think that is one of the reasons why you are seeing so many of the biotechnology companies forming partnerships with larger companies. They now recognize the cost of going forward, or commercializing. I was thinking more in terms of Federal support for the process side of it, in the training of people in the technologies that are going to be necessary for industry to have. Industry will do some of it as it works along. There is no question large industries can afford it, but when we are training engineers, for example, we have to recognize that those skills that are going to apply to a biological process are quite a bit different from those that would apply to a chemical process. I wouldn't say chemical areas are dead by any stretch of the imagination, but the growth areas for the employment of new people certainly lie in areas such as biotechnology.

Certainly, at the same time, it would be of great assistance I think, to the commercialization of biotechnology. That is really what I was thinking about. I think we have the basic research on the one hand, and then we have the forming industry of biotechnology on the other hand. It is still forming. Clearly it is not going to form on just basic research; it needs the whole gamut of skills. So I think that the Federal National Science Foundation Fermentation Process Center at MIT is a very wise thing. Perhaps another initiative that would be a good example is the NSF's program to establish computer ceters. Both the biotechnology process center and the computer centers will certainly impinge on the needs of these new industries, biotechnology in particular.

Mr. **WALGREN**. Do you feel that there is a real hinderance in the ability of companies to collaborate in the basic research area? I am trying to think. We passed some legislation here a year ago, so we attempted to make it clear that short of, I don't know what the magic words were, product development?

Dr. **MAC LACHLAN**. I think that that legislation was extremely helpful. What I was thinking about was in connection with developing one of the major areas where biotechnology will make it fundamental to cooperate among companies in treating complex diseases—I am talking about extracorporeal therapy. I think that is something that has been around a long time, kidney dialysis for an example, is simply an example. What I am thinking about, for example, is our program with Dr. Rosenberg's cancer treatment. You have to bring a lot of different technologies together to succeed.

Furthermore, you probably have to bring a lot of different proprietary technologies together to make the health treatment systems that I can visualize we will be seeing over the next 10 to 15 to 20 years. I am really asking to maintain an open mind in this area, because no one company is going to own it all.

I think it is quite different from the past. In the first place, look where research is being done; it is being done all over the world. In Du Pont we may do 200 million dollars' worth of research, but we are talking 10 billion dollars' worth of research going on right now. If that is going to be usefully presented to the public, it has to have a lot of collaboration.

Mr. **WALGREN**. It seems that we often, in discussion, find people worrying about the relationship between industries and universities. Do you see great difficulties in that, where the proprietary interests are antithetical to public interest, and is that more just what people are talking about, or are there real hurdles that create difficulties that you can anticipate down the road?

Dr. **MAC LACHLAN**. I think there are the same difficulties that we all have seen. There is no real change here. I think it is very important for industry to understand the different roles that are to be played, and that it would be very shortsighted for industry, to in effect, prevent college-to-college interactions, or to promote intense secrecy on university campuses. In the first place, the academics that I know wouldn't let that happen, but I think it is something that we worry about.

I feel—and I am speaking for a large company that has had a lot of experience that extends back really into the late 1920's, interacting with universities we are more used to it and we are not interested in changing the capability of the universities to provide the seed base for our developments. We fully recognize that. So, I would be concerned about it, but I think that it has received such an airing and that people have now understood better than they did, say 4 or 5 years ago when it became apparent there was going to be this pushing together because of the nature of biotechnology. I think there is less likely to be undesirable entanglement. On the other hand, I would say that industry has to remain enlightened and the university has to remain concerned about their roles.

Mr. WALGREN. Could you think of any way we could encourage that kind of contribution, to just free-ranging basic research that Dr. Brown was trying to foster in his small institute?

Dr. MAC LACHLAN. Yes; we are very supportive of Dr. Brown's institute and, as a matter of fact, several years ago, we talked among ourselves in Du Pont about a way we could support the postdoctoral, either on the first or second postdoctoral, and concluded the only way we could do this would be to get an outside committee, of very prestigious people, who would pick these candidates from an array of them. Then we discovered that we don't have to do this, that Dr. Brown had already created just that type of thing.

On the other hand, I think that we can only do so much. You have the Presidential Young Investigators Award; we are involved in that. That is a long-term commitment—3 years or is it 5 years—I can't remember anymore. This one is 3 years. So, when you are talking about fairly large sums of money, committing it for a period of time, means that you are limiting your flexibility in the future in case something different should come along. But, fundamentally, all of the support that industry provides to academia competes with research money that is to be spent internally on projects that can be specifically applied. So, it is a fundamental act of faith, when we preserve part of our total R&D budget for the universities.

I would say that the important idea is that governmental programs that help industry to have better justification for putting money into research in universities, as opposed to somewhere else, would be a good direction. For example, when the R&D credit came along several years ago, one of the arguments we used to use when we were talking about increasing research budgets was that it only costs 29 cents on the dollar. That sounds like a real deal, instead of 42 or 50 cents, depending on the tax rate. The things I think that are giving an incentive from a tax point of view that make R&D a lower percentage of budget is the direction I would look anyway.

Mr. WALGREN. Well, thank you very much for your contribution. We appreciate being able to talk to you about it.

[Questions and answers for the record follow:]

VP 10402

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SENIOR VICE PRESIDENT TECHNOLOGY

July 29, 1986

RECEIVED
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COMMITTEE ON SCIENCE
AND TECHNOLOGY

The Honorable Don Fuqua
U.S. House of Representatives
Committee on Science and Technology
Suite 2321 Rayburn House Office Building
Washington, D.C. 20515

Dear Mr. Fuqua:

I am writing this in response to your letter of July 16, 1986 as a follow-up of the hearing held on April 24, 1986. My views on the questions posed are as follows:

1. It has been suggested that the U.S. is losing its economic advantage with respect to scientific applications. To what extent is this the case in the transfer of biomedical research information to medical practice? What factors could benefit the rapid and efficient commercialization and application of biomedical research findings?

If by biomedical research findings you are referring to the products of modern biotechnology, I would say several concerns arise.

First, the lack of a clear regulatory pathway and understanding of which agency has jurisdiction over a particular development has been a problem. The recently published Coordinated Framework for Regulation of Biotechnology has been a very positive step. We believe this articulation of the Government's policy coupled with the cooperation among the agencies to regulate new developments should be given a good test before any new regulations are imposed.

A second concern, which is more worrisome at the present time, is the ability of special interest groups to block needed field testing of products that have been developed using the techniques of biotechnology. At the present time not much damage has been done, but we are certainly going to see many more requests for testing vaccines and other new products over the next several years. Proliferation of such blocking tactics could prevent scientists from obtaining the information needed to assess the safety and efficacy of the fruits of this technology. Special interest groups often have valid points as they challenge procedure for approving new products. However, we need to find ways to prevent objections based solely on form or on principle from slowing the approval and testing processes.

Third, the slow response of our regulatory agencies with regard to new drug approvals has the potential to place us at a disadvantage. This arises from understaffing, but also from great pressure to avoid risk. We need to be sure the agencies have enough people to efficiently handle the high priority new developments. We also need to develop approaches in the agencies that encourage decisive action, rather than inaction because of fear of adverse consequences.

Finally, the threat of unreasonable legal liability with high punitive damage awards in the entire drug area has real potential to deny the public many of the great benefits of new medical advances, or at least slow down the distribution of such products. I believe some cap needs to be put on punitive damages, and approaches developed to prevent liability from falling on the corporations with the "deepest pockets" rather than where the true fault lies.

2. There have always been a number of joint projects between research universities and medical centers. There is now a growing trend in biomedical research for more joint projects between universities and industry. To what do you attribute this? Will this recent trend in university-industry research arrangements continue for the short-term? For the long-term (20-25 years)? Can you determine what the impact will be for the university? For the industry?

The trend for joint projects between universities and industry is neither new nor is it limited to the biomedical field. For example, we have for decades maintained relationships with outstanding scientists in the area of polymer chemistry as well as other fields.

Relationships between universities and industry arise primarily from mutual need. Many of the new technologies like biotechnology, electronics, computers, and software development that are advanced by basic research in universities, are translatable in a relatively rapid manner to products and systems of industrial interest. This is somewhat in contrast to the past when much of what was done in universities was a long way from commercial potential. Another reason for closer ties is the great need these same industries have for more leading-edge understanding of the phenomena they are dealing with in order to remain competitive. In some cases, consortia among industrial partners and universities have been formed to jointly attack these problems. These relationships have important benefits to universities. By collaborating with outstanding industrial scientists new perspective is obtained by university faculty and students in such areas as goal setting, human needs, patent matters, and multidisciplinary cooperation. In addition, industry often has state-of-the-art specialized equipment that can aid the university researcher. And finally, such partnerships provide much needed funding.

I feel this is a long-term phenomena for the very practical technology transfer reason I mentioned above. I believe this is fundamentally a good trend as long as the universities still receive most of their basic research funds from the Federal Government. If adequate Federal funding is not forthcoming, our entire system will be reduced in quality with the ultimate loss in U.S. competitiveness because industry cannot make up for a significant shortfall of Federal funding.

3. The development of new technologies raises questions about who has control over a research project's results or data, i.e., its intellectual property. What is your view as an industrial sponsor of basic research at universities and other institutions? Does the property belong to the sponsor or the individual researcher? What problems do you see in the short-term? In the long-term? For protecting the rights of all parties involved?

This is a very complex question to answer generically because the disposition of rights to intellectual property will depend on what each partner brings to a project. As I discussed in my testimony, we have a number of projects in the area of biotechnology research where the university retains the rights to intellectual property or data. Thus, as regards basic research, I believe responsible industry recognizes it is best served if the intellectual property belongs to the university. The university can then benefit by licensing in a way that recognizes the sponsoring company(s) and at the same time develop approaches to allow the university researcher to share in the rewards.

In other circumstances, where we have specific questions that we need to have answered and the research to be done at a university builds upon work that we have done, we would expect that the fruits of such work would belong to us.

The best way to protect the rights of all partners involved and to avoid later misunderstandings is to have a detailed agreement before the sponsored research is started.

4. In your view, how long will it take for your basic research groups to be self-sustaining components so that research findings will be translated into products? What measures have you taken to assure that the products are unique from those supported by you at other institutions?

The time it takes for basic research to reach commercial profit generating products and processes varies enormously. As I mentioned under question two, for many technologies it is relatively easy to rapidly assess the commercial potential of new developments. However, even under such favorable conditions we expect that commercialization will take five years or more. On average, we project that basic research programs are usually carried out with a 10-to-20-year time frame in mind.

When we support research inside Du Pont, as well as outside, we carefully determine that the objectives are clearly understood by all concerned. We also monitor progress towards objectives on a reasonable frequency. These steps ensure we are making progress in collaboration with the researchers we have sponsored, and that we are not supporting the same activity in multiple organizations, including our own. When we sponsor specific projects outside Du Pont, we are electing to reduce our internal research budget in favor of the outside activity. This means we must ensure the outside effort contributes as effectively or more so, than does the work internally.

5. Dr. Berg commented on the Packard's committee report and its recommendation with regard to university-industry research agreements. To what extent, and in what way, should government policies provide stronger incentives for industry to conduct and support in-house and university biomedical research in the future?

I think government can be very helpful here. As I mentioned under question four, the level of research we sponsor outside is proportional to the value we perceive versus doing the same research inside. Clearly if it costs us substantially less to sponsor university collaborative programs, the amount we could justify would increase. However, whether the research is done in-house or at universities, I believe the government must do what it can to make it possible for industry to realize the profit potential from successful biomedical research. In view of the current regulatory hurdles, this may mean that the government needs to develop more streamlined permitting practices. Alternatively, it may be necessary to extend the term for patented research results or other mechanisms yet to be devised. In addition, recognizing that government's policy goals if achieved may not translate into markets of sufficient size to support a profitable business, further incentives may have to be provided. Such incentives could come in the form of tax preferences, more rapid depreciation of capital equipment involved in such relationships, and possibly other arrangements that reduce cost to the sponsor.

I hope that the above comments will be of assistance to the Task Force.

Sincerely,

A. MacLachlan

A. MacLachlan

Mr. **WALGREN**. Next we would be pleased to hear your perspectives, Dr. Williams.

[A biographical sketch of Dr. Williams follows:]

ALBERT P. WILLIAMS, PH.D.

Albert Williams earned his undergraduate degree in engineering from the U.S. Naval Academy in 1957 and subsequently served five years in the Navy on destroyers and submarines. In 1962, he resigned his commission to attend graduate school at The Fletcher School of Law and Diplomacy, Tufts University, where he earned masters degrees in international relations and economics, and a Ph.D. in economics.

In 1965, Dr. Williams joined the Bureau of the Budget, Executive Office of the President, as a staff economist and earned the Bureau's professional achievement award. In 1967, he moved to the White House Staff, where he served as an advisor on foreign assistance strategy until 1968, when he joined the Economics department of The Rand Corporation.

In the early 1970s, Dr. Williams became involved in research on academic medicine at Rand, and from 1975 to 1976, he directed a large study for the President's Biomedical Research Panel. In 1976, he took his current position as Director of Rand's Health Sciences Program. This is a large multidisciplinary health policy research program that currently employs 80 to 90 full-time equivalent professionals.

Dr. Williams' own research activities are currently quite varied. He is completing two studies involving academic medicine. One examines the strategies that academic medical centers have used to cope successfully with increasingly difficult environments, and the other compares the specialty choices and practice patterns of minority and non-minority graduates of the medical school class of 1975. He is also doing research on the effects of expanding physician supply on access to medical care, and on means of improving the information base for monitoring the Medicare Prospective Payment System.

Dr. Williams has been on the faculty of The Rand Graduate Institute since 1972. He has directed the Rand/UCLA Center for Health Policy Study, a joint program for training doctoral and post-doctoral fellows in health policy analysis, since it was founded in 1982.

Dr. Williams currently serves on advisory committees to the Congress' Office of Technology Assessment and to the American Hospital Association.

STATEMENT OF DR. ALBERT P. WILLIAMS, DIRECTOR, HEALTH SCIENCES PROGRAM, THE RAND CORP., SANTA MONICA, CA AND DIRECTOR, RAND/UCLA CENTER FOR HEALTH POLICY STUDY

Dr. **WILLIAMS**. I am honored to be invited to appear on this panel and to offer my thoughts on future biomedical research policy. As you know, my perspective is that of an outsider, one who has never been a bench researcher but has nonetheless had a longstanding interest in Federal biomedical policy. In particular, I shall comment on ways in which I believe that other developments in the U.S. health care system and other aspects of health policy are likely to impinge on biomedical research and the academic medical centers where much of it is conducted.

I foresee five major related factors as having important effects on biomedical research over the next decade: the pressure to reduce and control Federal deficits; persistent problems of controlling health-care costs; changes in health-care payment systems; growing alliances between academic medicine and the private, for-profit health-care-related industry; and generally increased budgetary stringency in academic medical centers. These will affect research funding, Federal policy, and the incentives that researchers face.

The pressure to control Federal deficits seems certain to continue well into the 1990's, which means that NIH and other Federal biomedical research budgets will remain very tight. Many proposals with scientific merit are likely to remain unfunded, the competition for existing funds will increase, and the search for new funding sources will become more intense.

Although substantial progress has been made in the control of health-care costs over the past several years, the problem is going to persist, and it may adversely affect biomedical research funding, independent of the general pressure it places on the Federal budget. Because advances in medical science often involve expensive new technologies, some regard biomedical research as one of the main causes of rising health-care costs. It follows from this line of thinking that one way to control costs is for the Government to spend less on biomedical research.

New payment systems, such as the Medicare prospective payment system, capitated payment plans, and preferred provider organizations, provide disincentives for the use of expensive new diagnostic and treatment modalities, unless they are cost-saving. Of course, there are some safeguards in these systems against inappropriate rationing of new technology, but it is difficult to design features that will only discourage wasteful use without also discouraging some use that is beneficial. As you know, there is currently considerable controversy about how best to pay for hospital capital costs under the Medicare PPS, and one of the important considerations is the potential effects on the development and diffusion of new technology.

One of the most striking changes in academic medicine over the past decade is in the attitudes toward relations with industry. When I first became involved in studies of biomedical research policy in the early 1970's, investigators who accepted money from a pharmaceutical industry to fund their research were generally regarded as having sold out. Today, almost all of the major academic research institutions already have or are exploring some form of agreement with the forprofit sector. Academe's abandonment of its doctrinaire attitudes toward industry seems like a very constructive change, but this change will profoundly affect the incentives facing faculty researchers and, perhaps, the willingness of traditional funders of biomedical research to continue their support.

Although the new alliances with industry promise to alleviate some of academic medicine's financial problems, there are few other promising opportunities on the horizon. There are many reasons to expect that budgets will become progressively tighter. The growing concern over the present or future excess supply of physicians seems likely to make public and private funding of medical education less generous. The Federal Government has already taken steps to cut back payments for the so-called indirect costs of medical education in Medicare's payments to teaching hospitals, and there are proposals to reduce reimbursement for direct education costs. Both demographic and economic factors are likely to reduce the demand for medical education and thereby make it difficult for medical schools to raise revenue by increasing tuition. Increased competition among all hospitals for patients will hold down the prices that teaching hospitals can charge for their services. Many teaching hospitals provide a disproportionate amount of care to Medicaid and charity patients; because funding for such care is becoming scarcer, teaching hospital budgets will be strained further. Finally, academic medicine will be forced to deal with the growing need to do more training in outpatient settings where there are no well-established means of covering costs.

The five factors outlined above seem likely to interact with one another to affect the biomedical research community in potentially adverse ways. I outline some of these below, not to play the role of a prophet of doom, but rather to suggest problems on which policy should focus in order to maintain the healthiest possible research enterprise, given resource and other constraints.

The following problem areas seem likely candidates for policy concern: supply of research funding, demand for research products, requirements for research support, allocation of research funds, and directions of research activity. Understanding their nature and origins seems essential to developing effective policy solution. The pressures from Federal deficits and difficulties in controlling health-care costs, combined with suspicions that research advances inevitably increase costs, will strengthen the hands of those who believe we spend too much on biomedical research. These arguments remind one of the Luddites, a group of workers in the early 19th century who tried to smash machines in order to prevent what they regarded as adverse consequences of mechanization. These latter-day Luddites, like their predecessors, are not entirely wrong in identifying some adverse effects of technological advance, but they too fail to balance costs against benefits and to seek ways to reduce the former and increase the latter.

Technological advances have been stimulated by the same forces that have led to spiraling health-care costs—reimbursement systems that almost unquestioningly paid for anything that the doctor ordered, no matter how uncertain or small the benefits. In the past, there were strong incentives for using expensive medical technologies, and this created demand for new drugs, devices, and procedures. Efforts to control costs cannot be effective without reducing that demand, and consequently, the demand for the basic and applied research that produces them. By no means are all advances in medical technology cost-increasing, and many cost-increasing advances produce benefits that are more than worth it. However, it is hard to determine in the early stages of development, much less at the basic research stage, how a new technological advance will affect health-care costs. This seems almost sure to make the development of new medical technology riskier business and the commercial payoffs of biomedical research more uncertain. Ironically, this change will be occurring at a time when academe and industry are developing effective ways to work together.

As funding becomes tighter for academic medicine and for the agencies that have supported it, the level of argument intensifies over cost burden-sharing. Academic medical centers produce much of their education, research, and patient care in what economists call a joint production process, such that it is impossible to separate all the pure costs of producing each product. As a consequence, there are joint costs that must be allocated in some rather arbitrary way to one of the products; there is no one right way to allocate these joint costs, only more or less acceptable ways to those who are asked to pay. The problem now is that all budgets are tight, and those who pay for academic medicine's various products are pressing hard to pay less of the joint costs. The current debates over ceilings on indirect cost reimbursement and over Medicare payment of medical education costs in teaching hospitals are manifestations of this. I do not wish to enter what I regard as being a largely unproductive debate over whether biomedical research has paid more or less than its fair share of these costs in the past. However, it seems unlikely to me that more of these costs can be shifted to the patient care or education dollar in the future. Thus, I see little prospect for getting more bang for the biomedical research buck than in the past.

The NIH peer review system has repeatedly withstood the attacks of its critics. No convincing case has been made for replacing it with another system for allocating research funds. However, I believe that it will face ever more difficult tests in the future because of the inherent difficulties of allocating scarce resources to an ever larger number of scientifically meritoricus proposals. In a period of more generous funding, the consequences of small mistakes in peer review were less. The pay line was such as not to exclude so many highly rated proposals, and chances were that if a solid proposal was not funded on first submission, it would be funded on the next. Almost surely that is no longer the case; there are simply too many solid proposals. Some believe that peer review will become more conservative in its judgments, choosing more established science in lieu of more innovative research. I think we don't know how the system will respond. I do believe that it is certain that its tasks will become more difficult at the same time that they become more important.

The new alliances between academe and industry offer many new opportunities for stimulating research, but it is clear that industry's criteria for supporting research will be different from those to which the biomedical research community has been accustomed in the past. Some biomedical discoveries can readily be commercialized because they involve patentable products or processes. Other at least equally important discoveries are in the public domain from the time they are reported, because they are in the nature of new understanding of physiologic or disease processes. Everyone working in the particular field of such discoveries benefits from the new understanding, irrespective of their support of the research that produced it. The new knowledge becomes a public good rather than a proprietary product. Industry benefits from both classes of discovery, but companies should have to answer to their stockholders if they do not show a preference for investing in research that is more likely to produce commercializable, proprietary goods. Industry, for example, would be less likely to have supported the basic research that earned Drs. Brown and Goldstein this year's Nobel Prize in medicine than research that promised to lead to new patentable drugs. My point is not that commercializable research is any less important to society but that the new opportunities for investigators to share more of the financial returns of such research will increase incentives to do more of it and less of research that produces knowledge for the public domain.

The problems I have outlined pose difficult challenges for Federal biomedical research policy and health policy, more generally. I make no pretense at having solutions, but I think it is possible to identify some areas in which policy initiatives will be required.

The multiple pressures on research and health-care budgets will make it even more important to have sound bases for determining which technologies are cost effective and in which circumstances. Despite the very impressive advances in medicine in recent decades, there is strikingly little hard evidence on the efficacy of much of the health care that is provided. And the Federal Government invests very little in technology assessment, despite its large investment in basic knowledge generation and the large burden of health care costs it bears. Unless we produce better information about the effectiveness of new technology and eliminate wasteful use, I fear that the latter-day Luddites will carry the day, reducing the use of technology and cutting the budgets for the basic research that generates new knowledge.

The success of health-care cost-control efforts will depend in part on their ability to reduce the wasteful use of expensive medical technology. Waste reduction is unexceptionable, but it is extraordinarily difficult to design payment systems that will not also discourage investments in technologies which have benefits that outweigh their costs, that may even be cost saving for the system as a whole, but not necessarily for the provider or the one who pays for the care. I expect there will be a continuing need to modify payment systems to ensure that they do not adversely affect important new technological developments.

I expect there is no better way to allocate biomedical research funds than on the basis of peer review, but that does not mean that the present peer review system is perfect. Indeed, even if it had worked perfectly in the past, it would work less well in the future because other things are changing. Therefore, I believe it will be important to analyze the process in order to improve it and to adapt it to future challenges. As funding becomes tighter, the consequences of peer review become more important. The review process is regarded by some as very expensive, but it may be necessary to spend more on it in order to achieve more efficient allocation of biomedical research resources.

The biomedical research community has long viewed with great suspicion any suggestion that the Federal Government should try to influence the direction of its research. Instead it has admonished Government simply to fund the best science, as judged by peer review. As long as NIH was the major funder of basic biomedical research, there was a strong case for such a laissez faire policy, but this situation seems likely to change as private industry plays a large role in funding academic research. NIH may need to be more attentive to balancing incentives for investigators. In particular, the financial incentives for institutions and individual investigators seem likely to attract more researchers to potentially commercializable pursuits, and NIH may need to focus more attention on ensuring that research that produces knowledge in the public domain is not short-changed.

Thank you.

[The prepared statement of Dr. Williams follows:]

Statement of

Albert P. Williams, Ph.D.

Director, Health Sciences Program
The Rand Corporation

Director, Rand/UCLA Center for Health Policy Study

before the

Science Policy Task Force
Committee on Science and Technology
United States House of Representatives

April 24, 1986

Mr. Chairman, members of the Science Policy Task Force, I am honored to be invited to appear on this panel and to offer my thoughts on future biomedical research policy. As you know, my perspective is that of an outsider, one who has never been a "bench researcher" but has nonetheless had a longstanding interest in federal biomedical policy. In particular, I shall comment on ways in which I believe that other developments in the U.S. health care system and other aspects of health policy are likely to impinge on biomedical research and the academic medical centers where much of it is conducted.

Factors Affecting Biomedical Research

I foresee five major related factors as having important effects on biomedical research over the next decade:

- The pressure to reduce and control federal deficits;
- Persistent problems of controlling health care costs;
- Changes in health care payment systems;
- Growing alliances between academic medicine and the private, for-profit health care-related industry; and

Generally increased budgetary stringency in academic medical centers. These will affect research funding, federal policy, and the incentives that researchers face.

Federal Deficits. The pressure to control federal deficits seems certain to continue well into the 1990s, which means that NIH and other federal biomedical research budgets will remain very tight. Many proposals with scientific merit are likely to remain unfunded, the competition for existing funds will increase, and the search for new funding sources will become more intense.

Health Care Costs. Although substantial progress has been made in the control of health care costs over the past several years, the problem is going to persist, and it may adversely affect biomedical research funding, independent of the general pressure it places on the federal budget. Because advances in medical science often involve expensive new technologies, some regard biomedical research as one of the main causes of rising health care costs. It follows from this line of thinking that one way to control costs is for the government to spend less on biomedical research.

Payment System Changes. New payment systems, such as the Medicare Prospective Payment System (PPS), capitated payment plans, and preferred provider organizations, provide disincentives for the use of expensive new diagnostic and treatment modalities, unless they are cost saving. Of course, there are some safeguards in these systems against inappropriate rationing of new technology, but it is difficult to design features that will only discourage wasteful use without also discouraging some use that is beneficial. As you know, there is currently considerable controversy about how best to pay for hospital capital costs under the Medicare PPS, and one of the important considerations is the potential effects on the development and diffusion of new technology.

Academic Alliances with Industry. One of the most striking changes in academic medicine over the past decade is in the attitudes toward relations with industry. When I first became involved in studies of biomedical research policy in the early 1970s, investigators who accepted money from the pharmaceutical industry to fund their research were generally regarded as having "sold out." Today almost all of the major academic research institutions already have or are exploring some form of agreement with the for-profit sector. Academe's abandonment of its doctrinaire attitudes toward industry seems like a very constructive change, but this change will profoundly affect the incentives facing faculty researchers and, perhaps, the willingness of traditional funders of biomedical research to continue their support.

Budget Stringency in Academic Medicine. Although the new alliances with industry promise to alleviate some of academic medicine's financial problems, there are few other promising opportunities on the horizon. There are many reasons to expect that budgets will become progressively tighter: The growing concern over the present or future excess supply of physicians seems likely to make public and private funding of medical education less generous. The federal government has already taken steps to cut back payments for the so-called indirect costs of medical education in Medicare's payments to teaching hospitals, and there are proposals to reduce reimbursement for direct educational costs. Both demographic and economic factors are likely to reduce the demand for medical education and thereby make it difficult for medical schools to raise revenue by increasing tuition. Increased competition among all hospitals for patients will hold down the prices that teaching hospitals can charge for their services. Many teaching hospitals provide a disproportionate amount of care to Medicaid and charity patients; because funding for such care is becoming scarcer, teaching hospital budgets will be strained further. Finally, academic medicine will be forced to deal with the growing need to do more training in outpatient settings where there are no well-established means of covering costs.

Effects of These Factors on Biomedical Research. The five factors outlined above seem likely to interact with one another to affect the biomedical research community in potentially adverse ways. I outline some of these below, not to play the role of a prophet of doom, but rather to suggest problems on which policy should focus in order to maintain the healthiest possible research enterprise, given resource and other constraints. The following problem areas seem likely candidates for policy concern:

- Supply of research funding,
- Demand for research products,
- Requirements for research support,
- Allocation of research funds, and
- Directions of research activity.

Understanding their nature and origins seems essential to developing effective policy solutions.

Supply of Research Funding. The pressures from federal deficits and difficulties in controlling health care costs, combined with suspicions that research advances inevitably increase costs, will strengthen the hands of those who believe we spend too much on biomedical research. These arguments remind one of the Luddites, a group of workers in the early 19th century who tried to smash machines in order to prevent what they regarded as adverse consequences of mechanization. These latter-day Luddites, like their predecessors, are not entirely wrong in identifying some adverse effects of technological advance, but they too fail to balance costs against benefits and to seek ways to reduce the former and increase the latter.

Demand for Research Products. Technological advances have been stimulated by the same forces that have led to spiraling health care costs -- reimbursement systems that almost unquestioningly paid for anything that the doctor ordered, no matter how uncertain or small the benefits. In the past, there were strong incentives for using expensive medical technologies, and this created demand for new drugs, devices, and procedures. Efforts to control costs cannot be effective without reducing that demand, and consequently, the demand for the basic and applied research that produces them. By no means are all advances in medical technology cost-increasing, and many cost-increasing advances produce benefits that are more than worth it. However, it is hard to determine in the early stages of development, much less at the basic research stage, how a new technological advance will affect health care costs. This seems almost sure to make the development of new medical technology riskier business and the commercial payoffs of biomedical research more uncertain. Ironically, this change will be occurring at a time when academe and industry are developing effective ways to work together.

Requirements for Research Support

As funding becomes tighter for academic medicine and for the agencies that have supported it, the level of argument intensifies over cost burden-sharing. Academic medical centers produce much of their education, research, and patient care in what economists call a joint production process, such that it is impossible to separate all the pure costs of producing each product. As a consequence, there are "joint costs" that must be allocated in some rather arbitrary way to one of the products; there is no one "right way" to allocate these joint costs, only more or less acceptable ways to those who are asked to pay. The problem now is that all budgets are tight, and those who pay for academic medicine's various products are pressing hard to pay less of the joint costs. The current debates over ceilings on indirect cost reimbursement and over Medicare payment of medical education costs in teaching hospitals are manifestations of this. I do not wish to enter what I regard as being a largely unproductive debate over whether biomedical research has paid more or less than its fair share of these costs in the past. However, it seems unlikely to me that more of these costs can be shifted to the patient care or education dollar in the future. Thus, I see little prospect for getting more bang for the biomedical research buck than in the past.

Allocation of Research Funds. The NIH peer review system has repeatedly withstood the attacks of its critics. No convincing case has been made for replacing it with another system for allocating research funds. However, I believe that it will face ever more difficult tests in the future because of the inherent difficulties of allocating scarce resources to an ever larger number of scientifically meritorious proposals. In a period of more generous funding, the consequences of small "mistakes" in peer review were less. The "pay line" was such as not to exclude so many highly rated proposals, and chances were that if a solid proposal was not funded on first submission, it would be funded on the next. Almost surely that is no longer the case; there are simply too many solid proposals. Some believe that peer review will become more conservative in its judgments, choosing more established science in lieu of more innovative research. I think we don't know how the system will respond. I do believe that it is certain that its tasks will become more difficult at the same time that they become more important.

Directions of Research Activity. The new alliances between academe and industry offer many new opportunities for stimulating research, but it is clear that industry's criteria for supporting research will be different from those to which the biomedical research community has been accustomed in the past. Some biomedical discoveries can readily be commercialized because they involve patentable products or processes. Other at least equally important discoveries are in the public domain from the time they are reported, because they are in the nature of new understanding of physiologic or disease processes. Everyone working in the particular field of such discoveries benefits from the new understanding, irrespective of their support of the research that produced it. The new knowledge becomes a public good rather than a proprietary product. Industry benefits from both classes of discovery, but companies should have to answer to their stockholders if they do not show a preference for investing in research that is more likely to produce commercializable, proprietary goods. Industry, for example, would be less likely to have supported the basic research that earned Drs. Brown and Goldstein this year's Nobel Prize in medicine than research that promised to lead to new patentable drugs. My point is not that commercializable research is any less important to society but that the new opportunities for investigators to share more of the financial returns of such research will increase incentives to do more of it and less of research that produces knowledge for the public domain.

Policy Implications

The problems I have outlined pose difficult challenges for federal biomedical research policy and health policy, more generally. I make no pretense at having solutions, but I think it is possible to identify some areas in which policy initiatives will be required.

Technology Assessment. The multiple pressures on research and health care budgets will make it even more important to have sound bases for determining which technologies are cost-effective and in which circumstances. Despite the very impressive advances in medicine in recent decades, there is strikingly little hard evidence on the efficacy of much of the health care that is provided. And the federal government invests very little in technology assessment, despite its large investment in basic knowledge generation and the large burden of health care costs it bears. Unless we produce better information about the effectiveness of new technology and eliminate wasteful use, I fear that the latter-day Luddites will carry the day, reducing the use of technology and cutting the budgets for the basic research that generates new knowledge.

Health Care Payment Systems —

The success of health care cost control efforts will depend in part on their ability to reduce the wasteful use of expensive medical technology. Waste reduction is unexceptionable, but it is extraordinarily difficult to design payment systems that will not also discourage investments in technologies which have benefits that out weigh their costs, that may even be cost saving for the system as a whole, but not necessarily for the provider or the one who pays for the care. I expect there will be a continuing need to modify payment systems to ensure that they do not adversely affect imortant new technological developments.

The Peer Review System

I expect there is no better way to allocate biomedical research funds than on the basis of peer review, but that does not mean that the present peer review system is perfect. Indeed, even if it had worked perfectly in the past, it would work less well in the future because other things are changing. Therefore, I believe it will be important to analyze the process in order to improve it and to adapt it to future challenges. As funding becomes tighter, the consequences of peer review become more important. The review process is regarded by some as very expensive, but it may be necessary to spend more on it in order to achieve more efficient allocation of biomedical research resources.

Priorities for Federal Research Funding. The biomedical research community has long viewed with great suspicion any suggestion that the federal government should try to influence the direction of its research. Instead it has admonished government simply to fund the best science, or judged by peer review. As long as NIH was the major funder of basic biomedical research, there was a strong case for such a *laissez faire* policy, but this situation seems likely to change as private industry plays a large role in funding academic research. NIH may need to be more attentive to balancing incentives for investigators. In particular, the financial incentives for institutions and individual investigators seems likely to attract more researchers to potentially commercializable pursuits, and NIH may need to focus more attention on ensuring that research that produces knowledge in the public domain is not short changed. Thank You.

DISCUSSION

Mr. **Walgren**. Well, thank you very much, Dr. Williams, and that raises some clouds for the future.

Do you think we can push research into more cost-effective medical technologies? Does it make sense to target dollars trying to reduce costs, as opposed to, I suppose, just the free-flow of funds into whatever new ideas come along?

Dr. **Williams**. I don't think we can or should try to influence basic research that way. I think it is important to do research on the technologies that we develop to determine where they can be used most effectively; such that, in effect, we won't waste the kind of technologies that we produce and, if you will, don't give new technology a bad name.

Mr. **Walgren**. I suppose the problem is if there is nobody that has an interest in doing it, if that is the case then it doesn't get done.

Dr. **Williams**. That is correct. The place where it is done in the Federal Government to a large degree is at FDA, but that focuses, if you will, largely on substances or increasingly on devices. The assessment does not really extend to how that substance or device is actually used in providing patient care. So really I think we require much more attention to research and trials on the full effectiveness of technology in the health care system, as used by the health care providers, so it is not so much assessing whether this thing can do what it says it does, or if this drug, if used that way, will be effective. But it involves, if you will, a look at the whole system to see whether the system is using it effectively.

Mr. **Walgren**. But then who would fund that, that sort of Government interest?

Dr. **Williams**. It really is not only a governmental interest, it is an interest of the third-party payers for care, because everyone who has to pay for care, including the individual, has a stake in insuring that the most is gotten from that health care dollar. The U.S. Government is the big payer in the sense that Medicare is the largest single payer, and the private sector tends to follow Medicare judgments of efficacy.

Those tend not to be made sharply in the sense that when magnetic resonance imaging was approved for use, it was approved for very general use. It remains to be seen whether it is cost-effective for all ways in which it will be used. For once the doctors are using it, once patients are asking for it, without knowing really, in some sense of what it provides, it will be difficult to control. It really is hard to perform sound technology assessment. It involves a very careful, phased approval or phased assessment of technology so that, as you learn that a particular use of technology is effective, then full reimbursement for that use is granted.

I am really concerned about, if you will, the false equation of medical research advances with cost increases in health care. I think as deficits persist, we will face more and more pressures not to use technology, and I think what we should try to do is not to use technology poorly.

Mr. **Walgren**. Do we give much of an effort to postmarket surveys as through FDA at this point? I am not very familiar with what the parameters are there. I gather with respect to drugs, it uses adverse reactions?

Dr. **Williams**. I think it is mostly on the negative side, yes. I think it is a very important thing. I think if we paid more attention to post-marketing surveys, we could have drugs available earlier. But I think we really need to pay more attention to how that substance is used, how the technology is used by the health-care provider. That is where very little research is applied, and the budgets for the agencies that provide it are really very skimpy.

Mr. **Walgren**. And we do rely mostly on the interested parties to pay for their research?

Dr. **Williams**. Yes.

Mr. **Walgren**. It is inhibiting to bring these things on, because if the interested party is conducting research you have to really be sure about it, I suppose, before you are willing to approve it, compared to if you were conducting it, or a true third party were conducting it, you might have more confidence in the result.

Dr. **Williams**. I think that we know enough about sound research design now that we can monitor sound research and the data collection. I think it doesn't make as much difference who conducts the research. What I think is, at this point, there is not a whole lot that can be done to assess a technology once it is out there; to do research to determine limits of its value is much more difficult then. The people who have incentives for that are those who pay the bill, and at this point not much research is funded by them, and, in fact, the budgets of Federal agencies in recent years have been cut back for that kind of research.

Mr. **Walgren**. You make an interesting point about the push toward commercialization that might come out of industrial alliances. Certainly, the incentives will be there and they would move in that direction, wouldn't they?

Dr. **Williams**. I believe they will, and that is the one area where I think the National Institutes of Health should be attentive in balancing incentives. I think it will be natural for the National Institutes of Health to move that way because I think they are producing knowledge. I think it is also the case that research that in the past was viewed as noncommercial is increasingly viewed as commercial. I think it is important not to shortchange other knowledge generation that is available to the general scientific community as soon as it is published.

Mr. **Walgren**. As that industrial incentive works its way into the proposals that came of the universities, then the peer review system is going to have to be even more vigilant to screen out to make sure that they are choosing the ones that are really the best on their merits as opposed to the one that somehow are not worth pursuing.

Dr. **Williams**. I must say I am less concerned about real merits than balance, because some of the research that industry will be happy to fund will be very meritorious basic science. What I am concerned about is that there are different domains of basic science, and that the incentives behind commercialization will suddenly cause biomedical scientists to shift their attention more to research that promises to lead to commercial, proprietary products, as opposed to research that may contribute enormously to the understanding of some basic disease but for which there are no property rights. So this is where I see a need for full vigilance to assure we don't shortchange research that is only going to produce knowledge in the public domain.

Mr. **WALGREN**. Well, thank you very much for your consideration. We appreciate it and we look forward to talking to you about issues in the future.

Dr. **WILLIAMS**. Thank you.

Mr. **WALGREN**. Thank you very much.

[Whereupon, at 1 p.m., the task force adjourned to reconvene on Tuesday, April 29 at 10 a.m.]

[Questions and answers for the record follow:]

SCIENCE POLICY TASK FORCE

Hearings on Policies for Biomedical Research

April 24, 1986

Followup Questions for Dr. Albert P. Williams

1. **With respect to considering future directions for Government policy in support of the biomedical sciences, what should be the respective roles of the scientist, the public, and the Government in the decision process for setting short- and long-term priorities in biomedical research? In public health?**

The scientist, the public, and the Government should have few fundamental differences in objectives with respect to the setting of priorities for biomedical or public health research. That is, each is presumably concerned with having research move in directions that are most useful for society. The problems in priority-setting and the differences between these three groups tend to arise because of the differences in their perspectives regarding the planning and predictability of scientific advance, and to the extent that advance can be predicted and planned, the practical consequences of having non-scientists involved in priority-setting.

Unfortunately, each group mistrusts the sophistication and the motivations of the other. The scientist generally fears that public or Government involvement in priority-setting will cause the Government's (and private foundations') resources to be wasted on research of little scientific merit, simply because it falsely promises advances in areas of high social concern. The public fears that scientists are too strongly motivated by parochial concerns and the vogues of their community and are relatively unconcerned about the practical applications of their research, particularly in areas of high social concern. The components of the Government are split according to their constituencies: agencies, such as the National Institutes of Health, which deal closely with the scientific community and regard themselves as part of that community, feel that research resources are best allocated on the basis of judgments by scientific peers. Other agencies, such as the Office of Management and Budget, tend to be concerned about the incentives that drive the scientific community and want a stronger role for themselves and the non-scientist in priority-setting.

I think that, in reality, public policy toward the support of biomedical and public health research would be improved by better communication and more collaboration between the scientific community, the public, and the Government. The public should try to articulate better and more specifically its priorities. Scientists should try to respond as specifically as possible regarding the avenues of research that offer the greatest promise to satisfy those priorities and should be very candid about the limitations of current knowledge. Government should focus on evaluating existing programs and developing new ones both to promote better science and to improve its contributions to the solution of high-priority problems.

2. **It has been indicated that it is often difficult to predict the next major breakthrough in research. From your perspective, is it a desirable, long-term goal that the U.S. maintain leadership in all fields of biomedical research, or should it be to build our strongest areas?**

In responding to this question, I think it is important to distinguish between research whose results are in the international public domain, virtually from the point of discovery, and research that yields proprietary benefits. For the former, which includes most of the research that the Federal Government seeks to fund, it should make very little difference to us where discoveries are made, and we should logically be as pleased with a breakthrough by foreign scientists as we are with one by U.S. scientists, except for concerns of national pride.

For the latter class of research, we need to be concerned about effects on the international competitive position of the U.S. It may make a lot of difference to the health of certain U.S. industries, such as pharmaceutical and medical technology firms, if other countries take the lead from us in certain areas. However, the Government has generally not been directly involved in funding this class of research, and we have relied on the profit motive to stimulate private initiative in this area.

We should certainly be concerned about maintaining an environment that is conducive to our keeping as fast a pace of advance at the frontiers of science as any country in the world. We currently enjoy a lead position in many, if not most, scientific areas, but the magnitude of that lead has decreased and will continue to decrease as other countries develop their scientific communities. Because of the nature of breakthroughs, we can expect to lose a few "races," to continue with the metaphor suggested by this question, but we should not allow ourselves to drop in the "overall standings." If we start dropping back, it should be a signal to us that something is wrong, perhaps in our science education, perhaps in the incentives we offer scientists, perhaps some other area.

3. **In your view, to what extent should criteria beyond science, such as specific national health needs and other societal goals, play a role in decision-making about biomedical research support?**

As indicated by my answer to the first question, I think health needs and other social needs should influence the way we spend public resources on biomedical science. This does not mean that we should fund mediocre science, just because it has some relevance to these needs. Nor does it mean that "applied" science should receive a higher priority than "basic" science. It does mean that both the needs and the quality of the science should receive weight in the decision process.

4. **In addition to the factors judged to be important for maintaining progress in biomedical research, what factors are important to assuring that we also reap the economic benefits of the ensuing technology? How can Government, academia, and industry work together more effectively to accomplish this goal?**

At this point, too little attention and too few resources are devoted to the assessment of the real, as opposed to the theoretical, value of medical technologies. In the absence of rigorous analysis to assess the value of new technologies and health care financing systems that insulate most patients from the financial implications of much technology use, we almost surely engage in uneconomic uses of medical technology. That is, when the value of doing something is uncertain, but someone else is going to pay the bill nonetheless, chances are the technology will be used. I think we need to mobilize public resources to assess the value of new technologies so that we won't waste collective resources -- either public or private -- on uneconomic and ineffective applications. Information about the effectiveness of new technologies is truly a "public good" on which we have spent too little.

I am not sure about the most effective and efficient way to finance the analysis needed to produce this information. Obviously, the producer of a proprietary technology reaps benefits from a positive finding of value, but many technologies, such as new surgical procedures, are not proprietary in nature. Those who pay the bills for medical care would pesumably reap savings from better information on the effectiveness of medical technologies because they would not pay for ineffective applications. Thus, it is difficult to determine exactly how the financial burden of technology assessment should be spread across the various classes of beneficiaries -- technology firms, Government, third party insurers, etc. -- it seems clear to me that the Federal Government would be a large beneficiary and a logical candidate for bearing a substantial share of the burden.

5. **From your perspective, how will present and future biomedical research and technologies impact on the cost of medical care? Who should bear the cost? What will be the overall consequences?**

How the new technologies impact on cost will depend on how well we are able to assess their value and eliminate ineffective and inefficient use. I expect and hope that research will yield new information and new technologies whose benefits to health will far outweigh what they add to the Nation's cost of health care. Some new technologies should also result in cost savings. I believe that those who currently pay for health care would be willing to pay the bill for such new technologies, if their value can be proven. Absent such proof, based on sound assessments, I expect there will be increasing reluctance to pay for new technologies or the research that produces them.

APPENDIX 1

Policies for Biomedical Research

Testimony
of
Edwin G. Krebs
President
American Society of Biological Chemists

for Inclusion in the Record of the
Science Policy Task Force
United States House of Representatives
Second Session, 99th Congress
29 May, 1986

As President of the American Society of Biological Chemists (ASBC), I appreciate this opportunity to comment on what policies for biomedical research this nation is, or should be, working under.

ASBC is a nonprofit scientific society with a membership of approximately 6,800 biochemists. The Society was founded in 1906, and publishes the *Journal of Biological Chemistry*, one of the premiere peer-reviewed scholarly journals in the life sciences. ASBC is one of the founding members of the Federation of American Societies for Experimental Biology, and counts 35 winners of the Nobel Prize among its current members.

More than 80 percent of our members are tenured faculty at American colleges and universities. Approximately 10 percent of our members work for the federal government, primarily in research laboratories, and the remainder work in the private sector.

If there is a single unifying theme in what follows, it is that the *individual researcher* is the heart of the extramural biomedical research enterprise in this nation today. The talent, intelligence, and creativity of individual researchers have for too long been taken for granted by funding agencies, the Congress, and even the universities that employ them. We at ASBC believe that the individual researcher needs a voice, and we try to supply it. In short, ASBC proudly represents individual researchers. Our policy suggestions, therefore, focus on what we believe would most benefit their interests.

Four broad areas of biomedical research policy are discussed below: 1) funding and organization of the National Institutes of Health (NIH); 2) the use of peer review to make research funding decisions; 3) the problem of facilities funding; and 4) indirect cost reimbursement, perhaps the most contentious policy issue facing the biomedical research community today.

The National Institutes of Health. The National Institutes of Health is the world's premiere biomedical research facility, and since its creation in 1937 has been responsible for improvements in the health of our nation's population that are little short of miraculous. NIH research has been responsible for development of sulfa drugs; insulin to treat diabetes; quinine to treat malaria; the heart-lung machine; the birth control pill; discovery of the role of DNA as the molecular basis of inheritance; the development of genetic engineering; development of the kidney dialysis machine; and many other advances.

Enclosed is a copy of "A Proposal for Fiscal Year 1987," published by the Ad Hoc Group for Medical Research Funding. This proposal, which ASBC has endorsed, discusses NIH's accomplishments over the last 50 years, and what it will take in the future to continue this level of progress. Page 15 covers the Group's recommendations for the year 2000. It is recommended that by that time, 50 percent of approved grant applications be funded, and that the research budgets for NIH and the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) rise 2-3 percent a year above the current services level until a level of funding one quarter to one third higher in constant dollars is achieved.

Of course, we realize that we are living in a period of budgetary restraint, and will be for the foreseeable future. The Group notes that:

"Scientists join all other segments of our society in their concern that [deficit spending and the growing federal debt] be reversed. However, we do not believe that sharply decreasing our nation's investment in research and development is the way to accomplish this goal. R&D investment fuels our economy, provides goods and products that are urgently needed to reverse the recent decline in the U.S. trade balance for high technology products, trains the scientists who will provide the new ideas in the next generation, and improves the health and job productivity of the American people. The means must be found to permit our nation to balance its budget while continuing its R&D investment in our future."

Congress and the Administration need to hold extensive consultations over the next few months (and in the future as needed) in order to agree on a funding level for NIH. It is not productive to go through an annual battle over this issue, which typically entails the Administration proposing a "no-growth" or less than no-growth budget, knowing that no matter how generous it is to NIH, Congress will add on large amounts of money in order to demonstrate that it is "pro-health."

While the biomedical research community appreciates Congress' support for NIH, this annual confrontation is very disruptive for many researchers, who spend each spring wondering if their approved grants will be funded. Many members of ASBC go through this each year, and it is not conducive to peace of mind, let alone to creativity.

Therefore, we hope Congress and the Administration can come to some meeting of the minds on this point before the fiscal 1988 budget is submitted. The important point in any agreement is that there should be a steady and moderate upward trend in constant dollars until the optimum level of funding is reached, which would occur around the year 2000 under the proposal of the Ad Hoc Group for Medical Research Funding.

Peer Review. One of the major foundations of scientific research policy in the United States is the use of peer review to evaluate what research is worth funding. One's scientific peers are, in most cases, best qualified to judge the merits of a particular research proposal. The effectiveness of the peer review system is evident from the dramatic improvements in the health of the American people over the past half century—due for the most part to applications of knowledge gained from peer-reviewed fundamental research.

Therefore, one should tamper with the peer review system only with great care. Unfortunately, such tampering is beginning to occur with increasing regularity. For example, much is made by some politicians of the supposedly inequitable "geographic distribution" of basic research grants. By this is meant the apparent concentration of basic research grants in certain areas of the country—California, the Boston/New York area, and Chicago, for example—while researchers at schools in other regions of the country have a difficult time getting funds.

To correct this, some politicians advocate a more "equitable" distribution of funds, to insure that less well-known schools receive their "share." Although the political appeal of this idea is undeniable, one hopes it does not receive widespread acceptance.

First, the idea is based on a false assumption—that distribution of research funds is not fair or equitable. Actually, according to Eric Bloch, Director of the National Science Foundation, when the distribution of research funds is compared to per capita population in the states, or to the number of research scientists in each state, the distribution of funds is much more equitable than is apparent just by looking at raw numbers of grants in each state.

Second, even if research funds were not distributed equitably among institutions of higher learning, this is not necessarily bad. The quality of research facilities (indeed, of researchers) varies among institutions; if one institution is better, why should it not receive more research money than another institution?

This is not to say that there are not specific circumstances where another method of making funding decisions may be appropriate. For example, young investigators, with innovative ideas but no proven track record, may need special consideration. Likewise, investigators from historically underrepresented groups in science research—in particular, minorities and women—should be given a bit of extra assistance, at least early in their careers until they prove their abilities. For these reasons, we support the various young investigator programs such as those at NSF, NIH and the Office of Naval Research, as well as similar programs aimed at women and minorities.

Nevertheless, our support for the peer review system in general is undiminished. It is very important that Congress not begin to think of basic research funding as something to be distributed like formula grants.

Facilities. Many reports and studies have been done in recent years detailing the growing problem universities face in trying to carry on research in aging and outdated facilities. It has been two decades since the last great "building boom" on college campuses, and the problem is a real one, which Congress and others are beginning to recognize.

Many have watched with some dismay over the past few years as more and more colleges and universities bypass the usual review process in their quest for money to build new facilities. While these funds are not necessarily research funds, the trend is worrisome.

The major facilities bill in Congress this term is, of course, H.R.2823, which establishes a "set-aside" from research funds to be used to construct or renovate facilities. Under the bill, if research budgets decline, the facilities money would be the first to be eliminated, the intention being to prevent erosion of research funds.

We appreciate Mr. Fuqua's serious effort to address this very real problem, but we are concerned about the bill's linking of facilities and research funding. Even though Mr. Fuqua clearly intends not to fund facilities at the expense of basic research, we believe that in future years, this intention will get lost in the complexities of the appropriations process; in addition, universities are not likely to accept quietly the deletion of facilities funds they were expecting. Thus, we recommend that funds for facilities ought to be contained in a separate appropriation, and not be tied to funding for research.

This is also, in our view, the problem with one of the major recommendations in the otherwise excellent National Academy of Sciences report, Academic Research Facilities: Financing Strategies. Recommendation F-1 would increase from two percent to five percent the use allowance for facilities allowed as a cost under OMB Circular A-21. Among other problems, this recommendation also links facilities funding to basic research funding. Again, a separate appropriation would be a better way to fund facilities construction.

Most of the other recommendations in the Academy report are worthwhile; in particular, recommendation F-2, which would establish an independent nonprofit corporation with a one-time $500 million appropriation for the purpose of funding facilities construction, is an excellent idea and one well worth exploring.

Indirect Costs. Few issues in biomedical research policy—indeed, in research policy in general—provoke as much heated argument as the subject of indirect cost reimbursmenent.

Federal reimbursement of the indirect costs of research is, in effect, a federal subsidy to universities. It is our view that this subsidy should no longer be tied to research grants, but instead be provided to universities as a sort of grant-in-aid. Such a system would also eliminate any need for effort reporting.

For this reason, the Council and Public Affairs Advisory Committee of the American Society of Biological Chemists support the proposed revision to OMB Circular A-21 that appeared in the Federal Register on February 12, 1986. The proposal would cap the indirect cost reimbursment rate for the four administrative cost pools in A-21 at 26 percent as of April 1, 1986, to be reduced to 20 percent on April 1, 1987.

At a hearing before the House Science Subcommittee on Science, Research and Technology on March 20, 1986, OMB agreed to delay implementation of the first stage of the cap until July 1, 1986. Since that hearing, it has been negotiating with various interested parties on "alternatives" to the original notice.

If these negotiations produce a workable alternative, we will be very pleased; the negotiations will have solved a problem some people have been working on for over two decades. However, we are not convinced that a solution equitable to all concerned is possible without some form of a cap on the administrative portion of indirect costs.

We are sympathetic to the needs of universities for funding, from whatever source, and can understand their reluctance to accept reductions in the amount of funding they receive from the federal government. Nevertheless, the legitimate needs of university administrators do not always coincide with those of the researchers who labor at their campuses.

The fact is that ever since the cap on indirect cost reimbursement was removed in 1966, the indirect cost rate has been increasing. According to Science magazine, in 1984, $1.7 billion out of $5.2 billion in federal academic research funds went to pay for indirect costs. At a few universities, the indirect cost reimbursment rate is 99 percent, while rates upwards of 60 percent are not at all uncommon. In the meantime, at NIH, less than one in 3 reviewed grants actually receives funding. Thus, we have a situation where indirect costs continue to escalate, while funding for basic research grants becomes harder to obtain each year.

We believe that this disparate situation is due in part to the fact that the needs of individual researchers—the spark plugs that drive the great engine of the federal government's extramural research enterprise—are somehow considered secondary to the needs of the universities that employ them. In many ways, this unfortunate situation is the fault of those of us who should have been speaking out more forcefully than we have been in recent years on behalf of the individual researcher. After all, universities have, for many years, powerfully and ably been making their case for receiving an ever-increasing share of research funds to pay for services only indirectly related to basic research. One does not blame them for this; this is what all interest groups do. Nevertheless, university administrators seem to have forgotten that they will collect no indirect cost funds at all, at any percentage rate, if their researchers are unable to get approved grants funded. This can no longer continue.

In short, the ASBC Council and Public Affairs Advisory Committee support a cap, at some reasonable percentage, on the amount of money the federal government should spend on the administrative portion of indirect costs.

The opportunity to comment on these important matters is appreciated.

PUBLIC AND SCIENTIFIC AFFAIRS BOARD
AMERICAN SOCIETY FOR MICROBIOLOGY

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May 29, 1986

The Honorable Don Fuqua
Chairman, House Committee on Science
and Technology
2321 Rayburn House Office Bldg.
Washington, D.C. 20515

Dear Chairman Fuqua:

The American Society for Microbiology (ASM) is pleased to respond to the House Committee on Science and Technology's invitation to comment on "Policies for Biomedical Research " as part of the Committee's comprehensive review of national science policy. The ASM is the largest single biological life science Society in the world with an active membership of over 34,000. ASM members contribute to the applied fields of infectious diseases, clinical microbiology, epidemiology, industrial fermentation processes, ecological microbiology, agricultural microbiology and food technology, as well as to the fundamental areas of molecular biology, immunology, genetics, virology, oncology, microbial physiology, environmental microbiology, mycology and host parasite interactions. ASM members are deeply involved in biomedical research and have a profound interest in issues which affect federal research policies.

The ASM believes that a strong scientific establishment is essential to the well-being of the nation. The U.S. stands preeminent in the world today in its commitment to uncovering basic knowledge in the battle against disease and in assuring the supply of well-trained scientists to carry out the research which is essential to the health and economy of the nation. This preeminence has been achieved due to strong government investments over the past 50 years in support of scientists to freely pursue long-term basic, nontargeted research, usually with unpredictable practical applications. The support of basic research continues to be essential to the development of new fundamental knowledge upon which private research and development are based.

Biomedical Research Funding
The nation's investment in basic biomedical research has paid off richly in terms of improvements in the length and quality of the lives of its citizens and in the birth of a new biotechnology industry. The following partial list, developed in part by the Ad Hoc Group for Medical Research Funding (1987 Proposal) describes just a few of the benefits to society resulting from the nation's investment in biomedical research over the past 50 years:

- penicillin as the first practical powerful antibiotic
- streptomycin to treat and often cure tuberculosis
- development of the Salk polio vaccine
- discovery of the role of DNA as the molecular basis of inheritance
- influenza vaccines
- systematic vaccination of children against diphtheria, whooping cough, tetnus, mumps, measles, rubella, haemophilus meningitis and polio
- the use of radiation and drugs as well as surgery to cure cancer

- reduction in the death rate from bacterial infections from 25% to less than 3%
- the ability to treat 200 of the 3000 described genetic diseases
- rapid discovery of the causative agents of AIDS, Legionnaire's Disease, Toxic Shock Syndrome
- recombinant DNA technology, as a valuable research tool to study genetic mutations and the way malignancies arise and to produce valuable new products both in medicine and agriculture
- breakthrough discoveries in the young medical field of immunology which is enabling physicians to assist the human defense against disease

A copy of the FY 1987 Funding Proposal for Health Research of the Ad Hoc Group for Medical Research Funding is attached since the Group has documented so well both the value and promise of biomedical research as well as its funding needs during this year of deficit crisis.

Despite the remarkable advances in scientific research and improved health care, the biomedical research enterprise has begun to experience difficulties and may even be reaching a crossroads. Current research funding does not support the level of activity required and it does not permit exploitation of the opportunities that have emerged in the biological sciences. The increasing numbers of high quality research ideas that continue to go unfunded demonstrate both the existence of additional scientific opportunities and the continued need for growth to take advantage of them. Under the present program, considerable instability and unpredictability have developed. The most serious consequences of this situation are:
1) Young ivestigators are discouraged from entering and/or developing in the academic setting;
2) The productivity of established investigators is disrupted through chance interruptions imposed by current levels of funding and by fluctuations from year to year in the number of new and competing research grants;
3) ~~Investigators are~~ discouraged from taking on the risks inherent in innovative projects; and
4) The overall continuity essential to the training of future research scientists is disrupted.

If the U.S. is to maintain its world supremacy in biomedical research, continue progress in improving the health of its citizens and preserve the momentum of discovery, the federal government must maintain a long-term commitment to stable and predictable support of basic biomedical research. Research in the life sciences must be viewed as a long-term investment, which should not be sacrificed in economically hard times. Biomedical research is anti-inflationary in the sense that it ultimately contributes to more goods, more jobs, higher productivity and lower losses of time and less agony from sickness and death. In addition, basic research has been shown to essentially more than pay for itself. Dr. Selma J. Mushkin, author of Biomedical Research: Costs and Benefits, did an economic analysis of biomedical research conducted between 1900 and 1975. She found that every dollar invested returned $13 measured in increased productivity due to longer life and less illness. Basic biomedical research also contributes to the economy by discoveries which benefit nonbiomedical industries.

Adequate funding is essential for the biomedical research enterprise. At a recent National Academy of Sciences (NAS) conference on "What Research Strategies Best Serve the National Interest in a Period of Budgetary Stress," the following conclusion was reached, "The nature of research makes it particularly vulnerable to instability in support. In particular, a field of research can suffer long-term damage if the best students and young talent are not attracted and retained. Active research teams, once disbanded, cannot easily reassemble. And loss of access to the most advanced equipment is often the difference between world-class and second-rate work." The ASM has recommended that Congress appropriate a budget of at least $6.079 billion for NIH in FY 1987 to sustain present research capabilities and avoid the problems caused by unstable funding. In future years we believe it will be necessary for Congress to provide modest but steady growth to take advantage of new scientific opportunities and available research talent. We estimate that it will be necessary for Congress to increase the NIH budget by at least 15 to 20% for each of the next 5 years. In addition to funding for the high priority areas of investigator-initiated research grants and training, Congress should provide new funding for the modern equipment and instrumentation that is so vital to carry out increasingly sophisticated research projects and for the needed renovations of older laboratories and animal facilities.

The Investigator-initiated Research Grant

In our view, among the various programs at NIH, the individual investigator-initiated research project grants remain the most important mechanism for the generation of new knowledge. The investigator-initiated research project grant or R01 is the life blood of the national basic biomedical research effort. We believe NIH's highest priority should be to fund R01 grants and to minimize year-to-year fluctuations in the number of grants. We are concerned, however, by the increasing tendency of the Congress to provide funds that are inadequate to support the number of research grants which are mandated. Because of chronic underfunding for basic biomedical research, and the effect of the Gramm-Rudman--Hollings cuts, both new and competing and noncompeting NIH grants are currently being paid at 10-15% below study section recommended levels. These cuts are of particular concern because they come on top of an already rigorous pruning that occurs during the peer review process in the study sections with respect to the direct cost part of the grant. This approach is intolerable in that grants are awarded to conduct specific research that cannot be done if the funds provided are inadequate. While we have recommended that no fewer than 6,100 new and competing grants be awarded in FY 1987, we have urged as strongly as we can that sufficient funds be allocated to adequately fund the number of grants mandated. To do otherwise would result in the further "downward negotiation" of the size of grants next year, and a point of diminishing returns in terms of research effort could be reached.

Research Training

A second critical need is the maintenance of NIH pre and post-doctoral training programs at levels recommended by the NAS. We believe research training is as essential as research programs and if the level of trainees falls below that recommended by the NAS, we cannot maintain an adequate national cadre of well-trained biomedical scientists able to fully exploit the findings of basic research for the benefit of the public. We currently see a decline in the number of Ph.D.s matriculating into the biomedical sciences at a time when, scientifically speaking, we are in the midst of an explosion of research opportunities in the biomedical sciences that is unparalleled in history. In order to take advantage of these opportunities, we must make sure that we continue to train adequate numbers of qualified young men and women for careers in biomedical research. Acquiring the skills necessary to conduct basic biomedical research requires a minimum of 6 years on the job training (approximately 4 years of predoctoral and 2 years of postdoctoral after the baccalaureate degree). The Institute of Medicine (IOM) Committee on Personnel Needs and Training for Biomedical and Behavioral Research's most recent data show a decline in bioscience Ph.D. production. The Committee wrote in its 1985 Report that the number of predoctoral trainees in the basic biomedical sciences supported in 1984 was 11% below the Committee's recommended level and "is on a steep downward slope." The Committee went on to state that in the next 5 years, a large number of faculty members will reach retirement and consequently the need for young faculty to replace them will increase. National Research Service Award (NRSA) training funds have declined since 1974, both in real terms and as a percentage of research expenditures.

We caution that maintenance of critical levels for grants and training, however, should not be accomplished at the expense of other meritorious programs at NIH, such as R&D contracts, centers, intramural programs, etc.

National Institutes of Health Research Policies

Although NIH is dependent on federal funding, it is essential to permit NIH to continue to sponsor the most meritorious research projects in a climate that is as free as possible of political considerations. Although we recognize that NIH must be responsive to the public's demand for results from the expenditure of public funds, we also know that science requires independence and elbowroom. The laws which established NIH have proven to be farsighted and beneficial, and we caution against precipitous changes in the enabling statutes for NIH which could result in less flexibility and greater fragmentation in the system. In the absence of compelling reasons involving origination within the affected agency, we recommend against the establishment of new institutes and the earmarking of funds for specific research programs. To be responsive to changes and opportunities in contemporary science and to continue to provide excellence in biomedical research, NIH must be given as much flexibility as possible and should not be subjected to micromanagement through excessive political control over scientific research decision-making.

We believe it would be a mistake to prioritize basic biomedical research because it is usually investigator-initiated and delves deep into fundamental processes, from which sometimes emerge new ideas and concepts in a largely unpredictable fashion. These new concepts may have wide ramifications, and they may be exploited by industry for the common good and applied to the solution of specific mission-oriented tasks through appropriate applied research and development. The recent manufacture of insulin for human use by one of the new biotechnology, recombinant DNA industries is perhaps a good example. These industries are based upon fundamental knowledge and concepts generated through basic research conducted several years ago by scientists who were studying the manipulation of bacterial genes. At that time, this research was rather far-out and not of great general interest. It certainly had no profit motive, and it could hardly have fulfilled a mission requirement for any federal agency. However, it provided basic information of various mechanisms to introduce bacterial genes into other kinds of bacteria, and more recently to clone animal genes in bacteria. Nevertheless, these ideas and information from basic research had to be applied specifically to bovine or human insulin to see if the genes for insulin synthesis could be introduced into bacteria.

We also believe that the allocation of federal funds for biomedical research should continue to be based on the scientific merit review of research proposals. The peer review system ensures that the most meritorious proposals are indentified and in this way enables the federal government to get the best return for its investment.

Indirect Costs

Finally, we are concerned, as are most other people involved in federal research, with the problem of determining indirect cost. Our concern is sufficient so that we have actually supported the effort of the Administration to place a one year cap of 26% on administrative costs. However, we are strongly opposed to the proposed decrease to 20% in FY 1987. We consider the number to have been arbitrarily determined. Rather, we favor an approach in which the recommendations on indirect costs of the Administration's own White House Science Council are taken into consideration and which would hopefully lead to more uniformity and equity in the determination of indirect cost rates at different institutions.

In conclusion, we believe that a strong scientific establishment, based on stable and predictable funding for research and research training, is essential to the well-being of the nation, and we recommend that Congress not attempt to deal with temporary budget shortfalls by mortgaging the nation's future in biomedical research. To quote from the White House Science Council's Panel report on The Health of U.S. Colleges and Universities, "Our universities today simply cannot respond to society's expectations for them or discharge their national responsibilities in research and education without substantially increased support....The strength of the nation in trade, defense, and health has been directly related to past investments in science and technology." We recommend that the Congress thoroughly review the White House Science Council's recommendations.

We appreciate the opportunity to submit these comments concerning some of the issues which you identified to assess policies for biomedical research. We would be pleased to answer any questions or to provide additional information.

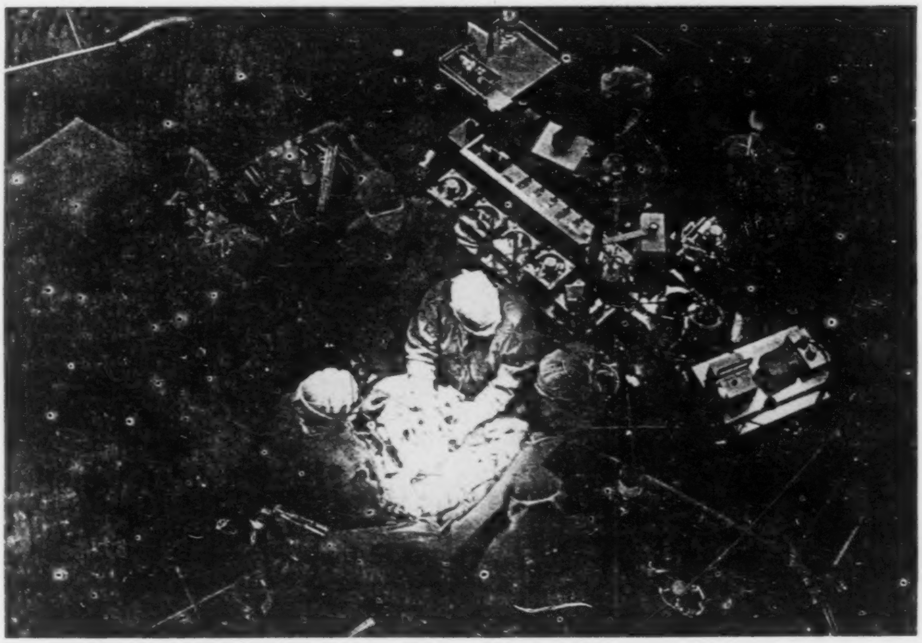
Sincerely,

H. O. Halvorson
Harlyn O. Halvorson, Ph.D.
Chairman, Public and Scientific
Affairs Board

Kenneth I. Berns
Kenneth I. Berns, M.D., Ph.D.
Chairman, Committee on Medical
Microbiology and Immunology

enclosure

The Ad Hoc Group for Medical Research Funding



Open Heart Surgery

"Replacement of damaged heart valves and coronary artery bypass surgery are now possible due to state-of-the-art surgical technologies developed in part through NIH-funded research."

A Proposal for Fiscal Year 1987

The Ad Hoc Group for Medical Research Funding

United by their concern for the vitality of the biomedical and behavioral research enterprise, a large and diverse group of organizations recommends that appropriations for health science be increased reasonably above Fiscal Year (FY) 1986 in the coming fiscal year. This document presents the rationale for this group's budget proposal for FY 1987.

Today, because there is a direct causal relationship between the work done in the nation's research centers and better health care, and because the Congress has recognized the benefits of increased investment in research, there is a revolution in the biological and medical sciences that is leading to the prevention and cure of countless previously intractable conditions. The pace of progress has placed the United States at the forefront of biomedical and behavioral research. Congress has demonstrated, through support of the NIH and ADAMHA, an acute understanding of the pace of research and the importance of a balanced research program.

In addition, the spinoffs of medical research are promising dramatic economic growth with concomitant benefit to the federal budget, the foreign trade balance, and the employment outlook. Biotechnology provides advances in human health, extraordinary possibilities for the industrial community, and the promise of reduced health care costs.

Yet this nation is confronted with a growing budgetary crisis engendered by years of deficit spending and the growing federal debt. Scientists join all other segments of our society in their concern that these trends be reversed. However, we do not believe that sharply decreasing our nation's investment in research and development is the way to accomplish this goal. R&D investment fuels our economy, provides goods and products that are urgently needed to reverse the recent decline in the U.S. trade balance for high technology products, trains the scientists who will provide the new ideas in the next generation, and improves the health and job productivity of the American people. The means must be found to permit our nation to balance its budget while continuing its R&D investment in our future.

© Ad Hoc Group for Medical Research Funding, 1986
Photos courtesy of National Institutes of Health

America's World Leadership in Medical Research and Biotechnology is No Longer Assured:

> *"Budgetary constraint is one thing, but manipulation without sensitivity to the consequences can destroy decades of effort to build a strong national biomedical capability."*
>
> Frank Press
> President,
> National Academy of Sciences
> April, 1985

West Germany and Japan continue to have the highest percentage of GNP devoted to national civilian R&D expenditures. For 1985, the R&D/GNP ratio for both West Germany and Japan was 2.6 percent; for the United States, 1.9.

National Science Foundation
Science and Technology
Data Book, 1985

Federal funds available for the purchase of academic research equipment and instrumentation declined 78 percent between 1966 and 1983.

Science Indicators
National Science Board
1985

From 1973–1982, the U.S. proportion of science and technology in biomedicine remained constant; its share of science and technology in clinical medicine and biology steadily declined.

National Science Foundation
International Science and
Technology Update,
January 1985

The Japanese government has targeted biotechnology as a key technology of the future.

Congress of the United States,
Office of Technology Assessment,
January 1984

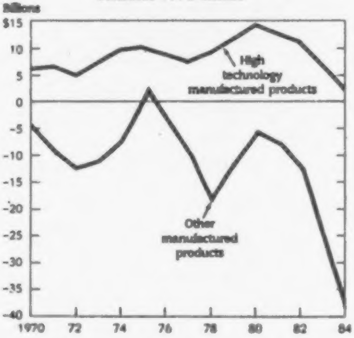
The U.S. trade surplus in high technology products, measured in constant dollars, fell by over 40 percent between 1980 and 1982.

Science Indicators
National Science Board
1985

Figure 1

U.S. trade balance[1] in high-technology and other manufactured product groups

Constant 1972 dollars[2]



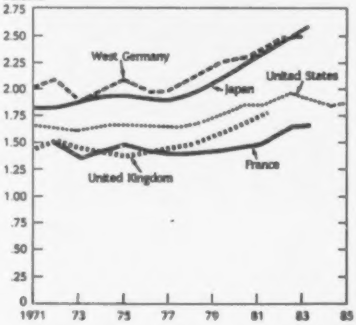
[1] Exports less imports.

[2] GNP implicit price deflators used to convert current dollars to constant 1972 dollars.

Science Indicators—1985

Figure 2

Estimated ratios of non-defense R&D expenditures[1] to gross national product (GNP) for selected countries



[1] National expenditures excluding Government funds for defense R&D.

Science Indicators—1985

The National Institutes of Health 50 Years and $50 Billion

- sulfa for the treatment of streptococcal infections
- routine use of insulin for diabetes
- discovery of Rh factor in human blood, its role in infant deaths and Rhogam therapy to prevent hemolytic disease of newborns
- penicillin as the first practical powerful antibiotic
- streptomycin to treat and often cure tuberculosis, followed by stronger drugs
- synthesis of quinine to treat malaria in WWII
- discovery of the role of Vitamin K in preventing or treating excessive bleeding
- identification of Vitamin D deficiency as the cause of rickets, leading to its prevention by supplementing milk with Vitamin D
- cortisone for control of rheumatoid arthritis and a host of other immune diseases
- the heart-lung machine, which made open heart surgery possible
- the birth control pill
- cigarette smoking identified as the cause of 85 percent of lung cancers
- development of the Salk anti-polio vaccine
- liver extract to treat pernicious anemia and later discovery of its active ingredient, Vitamin B12
- discovery of the role of DNA as the molecular basis of inheritance
- use of laser devices in human surgery
- the artificial heart and heart valves
- the development of knowledge and techniques that permit transplantation of the heart, lung, kidney, liver and pancreas
- use of beta-blocker and calcium channel blocker drugs to relieve angina
- influenza vaccines
- the advent of genetic engineering, which enables us to produce human gene products in the laboratory
- the development of coronary bypass surgery for atherosclerotic heart disease
- systematic vaccination of children against diphtheria, whooping cough, tetanus, mumps, measles, rubella, haemophilus meningitis and polio
- effective treatment to cure early syphilis
- adaptation of sonography from submarines to medical diagnosis, especially of fetuses
- dialysis to compensate for previously fatal kidney failure
- the use of radiation and drugs as well as surgery to cure cancer

was Established in 1937.
has Produced:

- Surgical and bioengineering technology enable us to provide freedom of movement for 200,000 bedridden or chairbound Americans each year through implanting new hips, knees, shoulders, wrists, elbows, and ankles.
- The death rate from bacterial infections has been reduced from 25 percent to less than 3 percent.
- Electronic pacemakers have been developed which control heart beat, preventing fatal arrhythmias, control breathing in persons with diaphragm paralysis, and may soon be able to control bladder function in 2.5 million paralyzed Americans.
- Insulin-deficient diabetics can be treated with pure human insulin produced with recombinant DNA techniques; insulin can be administered continuously through a portable pump; transplantation of healthy pancreatic tissue to restore insulin production is being tested, and the relationship of viral infection to pancreatic destruction is being unraveled and may lead to a vaccine to prevent diabetes.
- Mental illnesses, once poorly defined and somehow shameful, have been recognized as real illnesses that can be treated with a modern armamentarium of psychoactive drugs, bringing immense relief to individuals suffering from these diseases.
- Over 200 of the 3000 described genetic diseases can now be treated because we understand their basic cause and can compensate for the damaged gene product.
- New epidemics of infectious diseases such as Legionnaire's Disease, Toxic Shock Syndrome and AIDS have been discovered, their causative agents rapidly identified, and for each in turn an effective prevention or treatment has been rapidly devised and made widely known.
- Modern medical techniques permit us to open clogged arteries with balloon catheters, reattach retinas with lasers, repair knee joints through tiny incisions using the arthroscope, dissolve kidney stones with sound waves, reattach severed limbs, and maintain human life in the face of failure of any organ except the brain.
- More than half of burn victims suffering 60 percent body burns now survive because of careful management of fluid loss and infections and the recent development of artificial skin.
- The biologic and genetic basis of addictive disorders such as alcoholism, smoking, and drug abuse is being clarified and will lead to the development of effective therapies to release people from the bondage of addiction.
- Treatment of breast cancer has progressed from mutilative surgery as the only option to the use of limited surgery plus radiation. At the same time, chemotherapy has increased the survival rate for the 34,000 women afflicted yearly with this common female cancer.

Premature Infant

The outlook for a premature baby born in the 1980s has dramatically improved compared to a premature baby born 50 years ago. Life saving medical research and technology not only can help the newborn infant survive the first crucial months of life: they also allow him to grow to maturity and lead a healthy, prolonged life.

Why Federal Investment in Medical Research Must Be Increased

> *"If you are looking about for examples of things that government can do, and do beautifully well, rest your eyes on the NIH. The existence of this institution in its present form owes much to the political leaders in and out of Congress, whose wisdom and statecraft put it in place."*
>
> Lewis Thomas, M.D.
> Lasker Foundation Awards
> 1986

- 855,000 Americans are diagnosed *each year* as having some form of cancer; about half will die of the disease.
- 3.5 million Americans are disabled by stroke or other injuries to the central nervous system.
- 2 million elderly Americans are afflicted by Alzheimer's disease.
- 60 million people suffer from cardiovascular disease.
- 16 million Americans have developed osteoarthritis.
- 11 million people in this country are diagnosed as having diabetes.
- 100 million Americans suffer from some form of digestive disorder each year.
- One of three babies born in 1985 will develop cancer during its lifetime.
- 100,000 Americans will die this year as a result of allergic and infectious diseases.
- 2.5 million new cases of gonorrhea and over 80,000 new cases of syphilis develop each year in the United States.
- 62,000 people each year become blind. At any one time there are over a half a million blind people in America.
- 24 million Americans in any given month are afflicted by psychiatric disorders.
- 4,000 infants died in 1981 in this country as a result of respiratory distress syndrome.
- 7 million visits to physicians' offices due to blood diseases were made in 1979 alone.
- 15 million Americans suffer from chronic lung disease.
- Over 200 million Americans have at some time contracted a dental disease.
- About 2 million children in this country have mental disorders so severe they require immediate care.
- 17 million hearing impaired persons live in the United States.
- 300 million people worldwide are afflicted with malaria; each year 1 million will die of the disease.
- Each one of the approximately 240 million Americans will at one time or another suffer a disorder of the endocrine system. Endocrine diseases range from osteoporosis to diabetes and include hypertension, hormonal dysfunction, growth and development disorders.

Ad Hoc Group for Medical Research Funding: A Proposal for the National Institutes of Health

FY 1986 Congressional Appropriation	FY 1987 Current Services	Ad Hoc Group FY 1987
$5.498 billion	$5.993 billion	$6.079 billion

This proposal brings the increase for the NIH into line with those requested by the President for science support in other agencies, excluding the larger increase for the Department of Defense (see Figure 3). It provides very modest program growth of about $86 million or 1.4 percent over a current services budget (which includes $15.6 million for nursing programs recently transferred to NIH).

The FY 1987 Ad Hoc Group proposal for NIH provides funds sufficient to support research activities at levels provided for by the FY 1986 congressional appropriation, with modest increases for a variety of important programs. Our proposal emphasizes the need for program balance at NIH with a diversity of support mechanisms and recognizes the multi-faceted mission of the agency — to conduct basic and applied research, train qualified promising investigators, and speed the transfer of life-prolonging and life-saving research and technology to the public. Our proposal also emphasizes the high degree of flexibility required in the management of NIH for the greatest effectiveness in the use of research funds, considering the substantial variations in the pace of research in different fields supported by the various institutes.

The Ad Hoc Group's proposal for NIH has been severely tempered by the stark realities of the current federal budgetary imbalance. The proposal does not, therefore, advocate optimal funding for NIH; substantial additional funds could be efficiently deployed immediately over a wide range of activities.

The Ad Hoc Group proposal for FY 1987 provides for:

- a current services dollar level for full funding at study section-recommended levels of competing and non-competing research project grants (approximately $3.4 to $3.6 billion).
- some growth in research career awards and funds sufficient to raise the current level of research trainees to that recommended by the National Academy of Sciences.
- needed upgrading and renovation of primate centers and outmoded and inefficient research laboratories.
- some additional funding for General Clinical Research Centers (GCRCs) to facilitate the conduct of clinical research projects and trials.
- a slight increase in the number of research centers: specialized/comprehensive, biotechnology, etc.

For the remainder of NIH's research activities — contracts, biomedical research support grants (BRSGs), minority biomedical research support, intramural research and full-time equivalent (FTE) personnel — we propose maintenance levels as established in the FY 1986 congressional appropriation.

Ad Hoc Group for Medical Research Funding: A Proposal for the Alcohol, Drug Abuse, and Mental Health Administration*

FY 1986 Congressional Appropriation	FY 1987 Current Services	Ad Hoc Group FY 1987
$366 million	$405 million	$465 million

The proposal for ADAMHA reflects the magnitude of the Agency's mission by providing necessary program growth over the FY 1986 level-of-effort. Our recommended funding levels are consistent with the recommendations of the Institute of Medicine of the National Academy of Sciences for a doubling of the ADAMHA research budget over the 1986 to 1991 period. This increase is necessary to achieve catch-up growth in the funding of mental health and addiction research. The FY 1987 current services budget of $405 million merely restores ADAMHA purchasing power for research and training to the constant dollar level of 1974.

The FY 1987 Ad Hoc Group proposal for ADAMHA allows funding sufficient to conduct biomedical and behavioral research activities at levels only modestly in excess of the FY 1986 congressional appropriation, with necessary increases for an array of critical programs. Our proposal emphasizes the need for program balance and recognizes the multi-faceted missions of the agency—to conduct basic and applied research, train qualified promising investigators, and speed the transfer of life-prolonging and life-saving clinical knowledge and technology to the public. Our proposal also stresses the high degree of flexibility required in the management of ADAMHA for the greatest effectiveness in the use of research funds, given its diverse research funding mechanisms. We urge ADAMHA to continue to use its multiple support mechanisms in recognition of the many ways in which excellent research can be organized.

The Ad Hoc Group proposal for FY 1987 provides for:

- necessary expansion in the level of competing and non-competing research project grants with full funding at study section-recommended levels (approximately $243 million).
- critical growth in research centers (including sufficient funding for competing renewals); Research Scientist Development Awards (which particularly focus on establishing a pool of talented young investigators); and funds sufficient to raise the number of research trainees to that recommended by the National Academy of Sciences.
- needed renovation of outmoded research laboratories and equipment.
- necessary funds for the intramural programs to provide for replacement of obsolete equipment and to regain lost positions.

This proposal recognizes the extraordinary contributions of ADAMHA-supported research and would hasten the growth and refinement of new knowledge and clinical applications.

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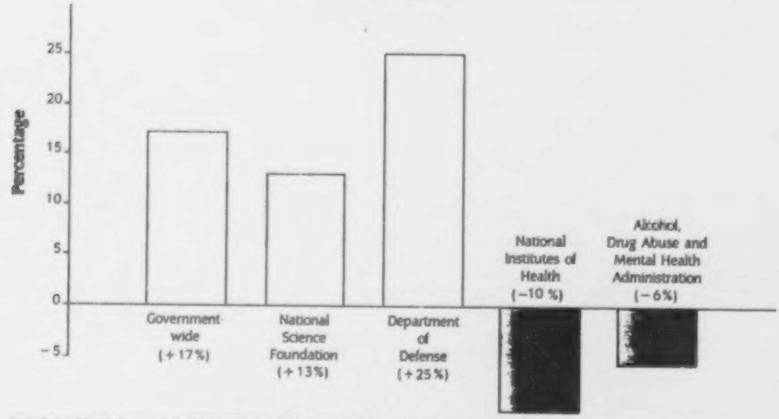
*Research and Research Training only

Figure 3

Federal Support for Research and Development
Percentage Increases
Fiscal Year 1987 vs. 1986
Obligations



Source: Budget of the U.S. Government, FY 1987 Special Analysis K. ADAMHA data adjusted to exclude Community Programs in accordance with stated congressional preference.

Figure 4

Percentage of Grant Applications
Recommended for Approval by Council
and Percentage Awarded, NIH, 1972–1986

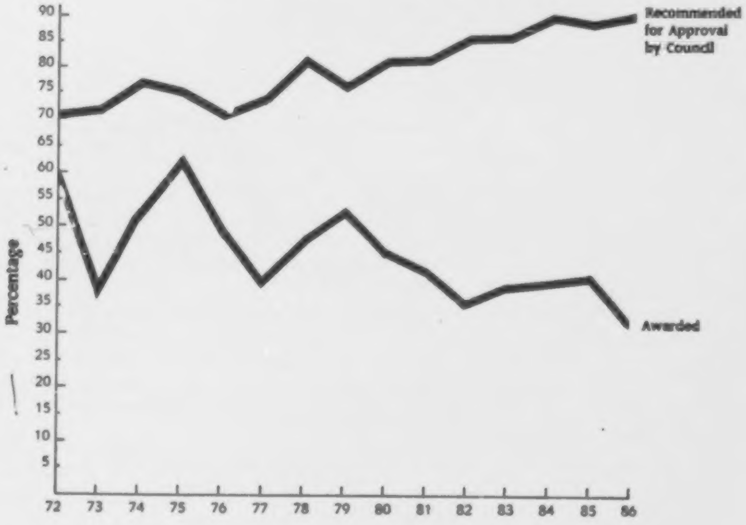
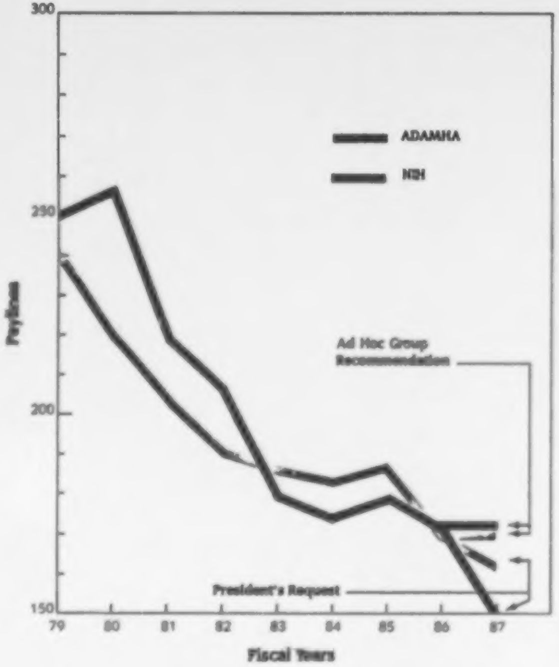


Figure 5

Paylines* for Funding Approved New and Competing Research Projects

FYs 1979–1987

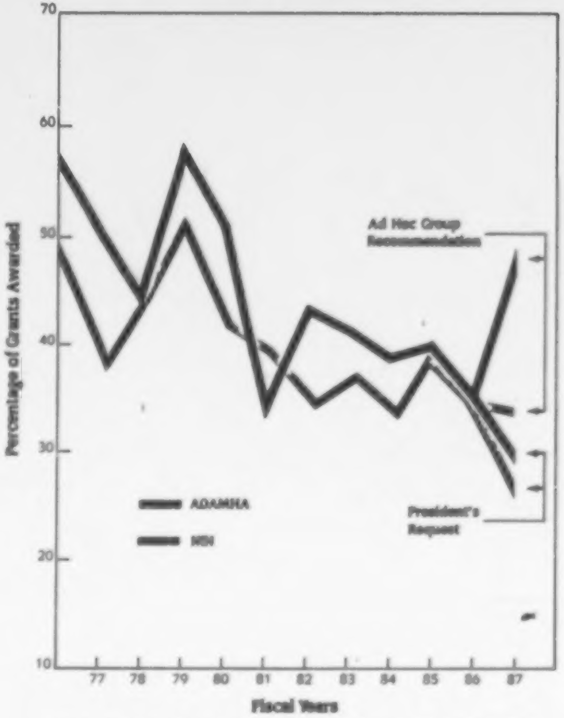


*In the NIH and ADAMHA merit review systems, the best proposals receive the lowest scores, and funds are awarded based on these priority scores. The "Payline" is the cutoff score or ceiling at which funds available for the fiscal year are exhausted.

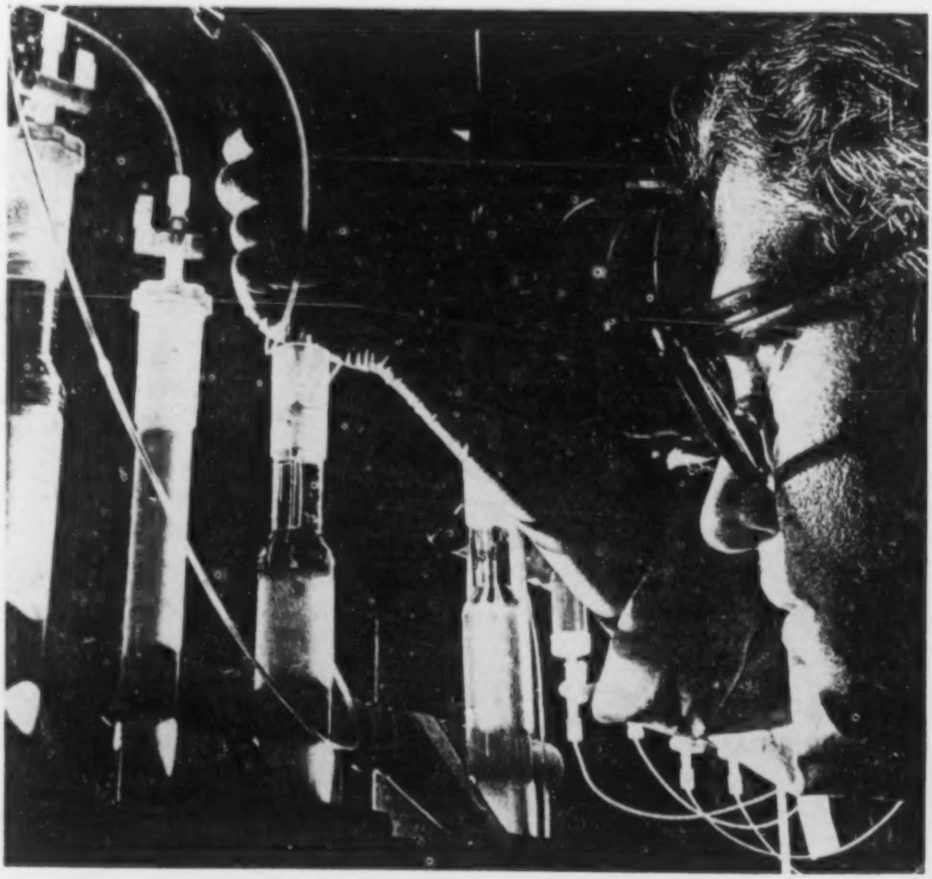
Figure 6

Award Rates* for Funding Approved New and Competing Research Projects

FYs 1976–1987



*Award rates are the number of projects actually funded as a percentage of those approved and therefore eligible for funding.



Small Scale Chromatography

A scientist uses small scale chromatography, in which a protein produced by recombinant DNA technology is run through small columns of densely packed materials especially designed to purify the desired protein.

Reasonable Funding of Medical Research Would Enable Pursuit of Opportunities Such as:

- Further study of the body's main defense mechanism against disease, the immune system. Disorders of the immune system occur in allergic diseases, certain forms of arthritis, multiple sclerosis, chronic infections, blood disorders, and other diseases, and are believed to occur in over 30 million people at some time during their lives.
- Evaluation of LAK cell and interleukin-II therapy of solid tumors. Early trials have shown promising results against such treatment-resistant metastatic cancers as melanoma and colon cancer.
- Efforts to develop effective vaccines against AIDS.
- Studies using a newly developed model of Parkinson's Disease in primates to devise new and more effective therapies for this movement disorder affecting 1 in 600 older Americans.
- Research to identify biologic clues in depression and mania, disorders which affect between 10 and 14 million people at any one time. Biologic clues are potential keys to explaining causes of depression, distinguishing among depressive patients, and selecting treatments best suited to their needs.
- Development of antibodies against the principal bacteria responsible for dental plaque and tooth decay. Although the incidence of tooth decay is declining, the average American child develops 11 cavities by age 17.
- Understanding how the clotting enzyme thrombin interacts in patients, which would provide important information on how the early events in clotting take place. This work has important implications for heart attacks, stroke and other abnormal clotting situations.
- Understanding how embryonic development is controlled genetically, which will provide valuable information on birth defects and malformations and perhaps how to prevent them.
- Use of monoclonal antibodies to treat cancer and to produce immune suppression for transplant recipients.
- Testing of plasmapheresis for treatment of Guillain-Barre syndrome, a form of ascending motor paralysis which follows viral infection in 2 per 100,000 persons.
- Development of drugs that might interfere with the release of cholesterol into the blood stream, thus reducing coronary atherosclerosis and the risk of heart attacks.
- Trials of an experimental herpes vaccine which has been successful in preventing development of latent herpes infection in mice.
- Development of effective prenatal diagnosis of cystic fibrosis based upon use of the genetic markers which have recently been identified near the cystic fibrosis gene on chromosome 7.
- Identification of the mode of genetic transmission in schizophrenias and affective disorders.
- Continued long-term testing of hundreds of new drugs and chemicals introduced into our bodies and the environment annually.
- Identification of the biological mechanisms involved in susceptibility to alcohol addiction.
- Research to identify further causes of low birth weight, which is associated with higher infant death and developmental disability rates and occurs twice as frequently in black as in white infants.

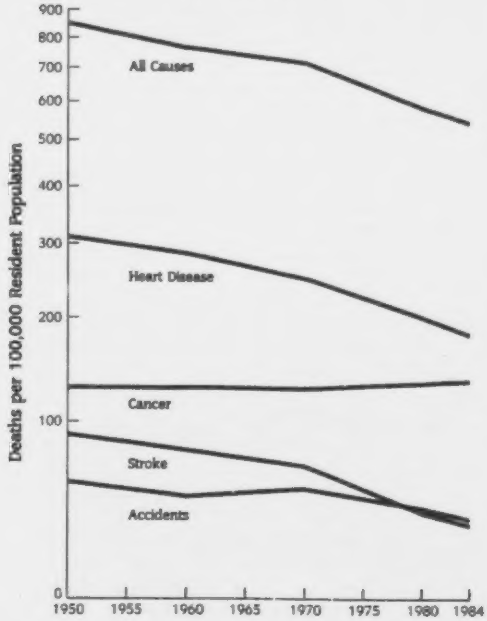
Economics of Medical Research At a Glance:

> *An overwhelming majority of Americans believe that "government funds for basic research should be increased by a sizable amount—even in this era of tight federal budgets and soaring deficits."*
>
> A Louis Harris Poll
> Quoted in *Science*
> December 1983

- Total health care costs in the U.S. for 1985 are estimated at $456.4 billion; federal investment in medical research is only 1.2% of this figure. Health care now consumes 10.8% of the GNP.
- The annual expenditure on health care in the United States is $2,000 per person. The annual federal investment in medical research to reduce this cost is only $25 per person.
- Studies show that the rate of return on every $1 invested in medical research is $13. Between 1900 and 1975, benefits exceeded the federal investment by some $300 billion in constant dollars, a seven-fold return.
- Over $40 billion is contributed annually to the GNP from medical research discoveries that are now used in non-health related products. This is more than the total federal investment in life sciences basic research over the past 50 years.
- More federal dollars are spent on the defense R&D budget in 15 months than the total spent on biomedical research since the establishment of NIH ($50 billion since 1937).

Figure 7

Mortality rates for the United States, for all causes of death and for four major causes of death, 1950–1984



Source: National Center for Health Statistics

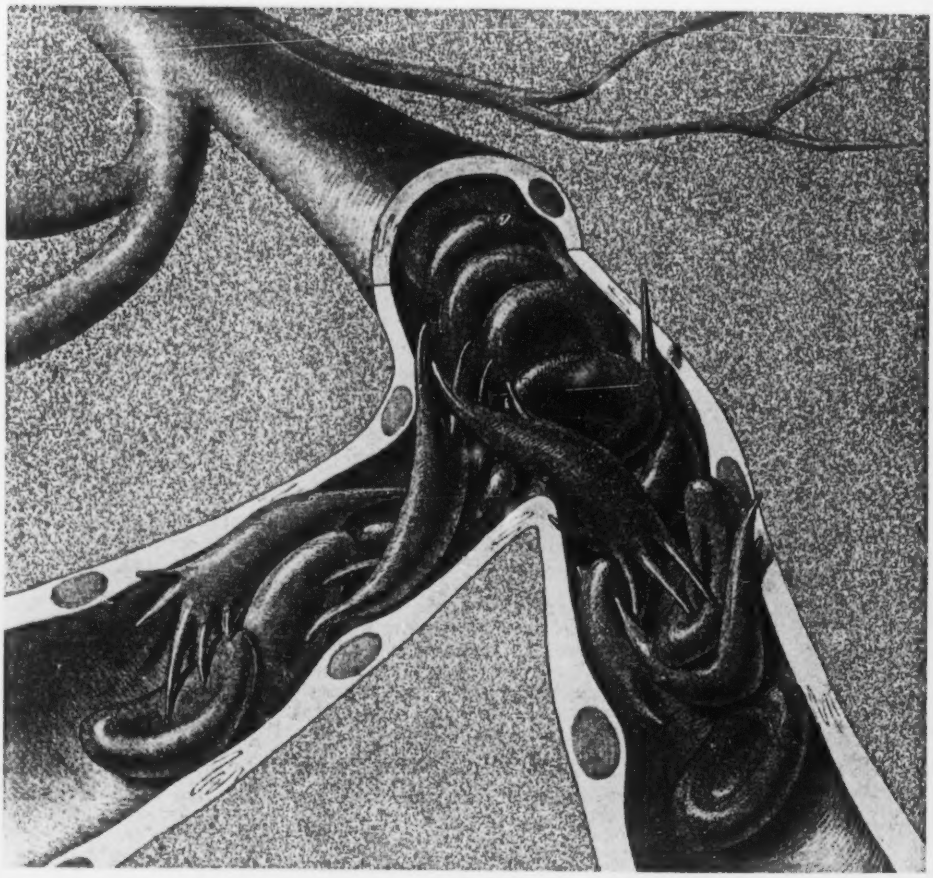
Ad Hoc Group Proposal for the Year 2000

The NIH and ADAMHA are the flagships of our nation's biomedical and behavioral research effort. They are unique in the world. They provide leadership and quality control as well as funds for scientists in universities and independent laboratories throughout the nation, and their own laboratories produce some of our finest research. Their administration is non-political, professional and dedicated. To maintain this world leadership and to continue to pursue the goal of advancing knowledge to alleviate human suffering, federal support for biomedical and behavioral research must have three characteristics:

- It must be on a stable base of federal funding which enables scientists to plan for the future so that they can pursue long-term basic research projects. Such projects are high risk, without clear immediate payoff, but they have the highest likelihood of ultimately improving health.
- It must provide a stable program for research training to ensure that we continually invest in those superb young people who will provide the creative ideas for the next generation of research. The time line is long for the advanced training necessary to equip a scientist for the sophisticated research of the year 2000.
- It must provide program flexibility. Scientific activity continually identifies the next attainable horizon, as research proceeds from one discovery to another. The focus of support should be on talent and creativity rather than rigid priorities and precise directions, which must always be limited to what is already known.

A stable base of funding will be achieved when we have assured a steady supply of new creative researchers who enter productive careers; supported the best ideas they propose, as judged by merit review and award of the top 50 percent of approved grant applications; insured that retiring scientists are replaced to achieve a steady-state; and provided proper equipment and facilities for this cadre of scientists to pursue their proposals. It is estimated that an optimal steady state will be achieved when the federal research effort is one quarter to one third larger in constant dollars than at present. Federal funding policy should be to increase the annual appropriations for both NIH and ADAMHA by 2–3 percent in real growth above the current services budget base for that year. Thus, the constant dollar budget base for each agency would be 25–35 percent greater by the year 2000 than at present. In this way we will fully unleash the creative potential of the biomedical and behavioral research enterprise.

Our reward will be the good health of not only our citizens but those of all the world, a vigorous industrial base in biomedical science and technology, increased productivity due to improved health of our workers, and the maintenance of our preeminence in health research.



Sickle Cell Anemia

Pictured above are abnormal elongated sickled red cells blocking the flow of blood in a capillary (normal red blood cells appear round). In recent years NIH has undertaken important research initiatives to develop prenatal diagnosis and effective treatment for sickle cell anemia.

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AMERICAN LUNG ASSOCIATION
The Christmas Seal People ®

Statement

of the

American Lung Association

and the

American Thoracic Society

to the

Committee on Science and Technology

of the

U.S. House of Representatives

Re: Policies for Biomedical Research

May 30, 1986

National Headquarters: 1740 Broadway, New York, N.Y. 10019 • James A. Swomley, Managing Director

The American Lung Association (ALA), and its medical section, the American Thoracic Society (ATS), appreciate the opportunity to respond to the Committee's request for a statement on biomedical research for the record of the Science Policy Study. The ALA has a long standing interest in federal biomedical research policies as they provide the major initiative for the control and elimination of human disease, including diseases of the lung. Established in 1904 to combat tuberculosis, the ALA is the oldest voluntary health agency in the United States. Our goal now encompasses the control and prevention of all lung diseases.

Our perspective is, perhaps, unique as a result of our longevity and the differences over time in medical practice and research. We have experienced the process of periodic reevaluation and substantive change in mission, orientation, and strategy. The ALA is broadly representative as our base is in the volunteers of a nationwide network of local service organizations. Our professional constituency goes far beyond the ordinary confines of medical research and extends into areas of public health, industrial and environmental safety, and preventive medicine. Finally, our mission is more important than ever. Lung diseases, including lung cancer, are the third leading cause of death in the United States. Tragically, while death rates from cardiovascular disease and cancer outside the lung are plateauing, or declining, death rates from diseases of the lung are increasing rapidly.

The following comments draw on two ALA organizational documents: (1) Report and Recommendations of the Task Force on Federal Lung Research (May 1982) and (2) Statement for the Institute of Medicine Study on the Organizational Structures of the National Institutes of Health (September, 1983). These statements remain largely applicable today and are therefore appended to this statement.

1. Management of Federal Biomedical Research Programs

A. General Organization

Research on the lung is conducted by a variety of federal agencies and also within the National Institutes of Health. They differ in authority, mission, scope, and strategies. The major agency involved in lung research, the National Heart, Lung and Blood Institute, has bureau status and is organ oriented. The National Institute of Allergy and Infectious Diseases and the National Cancer Institute are disease oriented, while the National Institute of Child Health and Human Development, the National Institute on Aging and the National Institute of Environmental Health are discipline oriented. Outside of the NIH structure are important organizations such as the Centers for Disease Control, the Environmental Protection Agency and the Veterans Administration.

The authorization of bureau status for the National Heart, Lung and Blood Institute allowed for expansion of their programs and a comprehensive and coordinated "mix" of basic science, clinical research, and demonstration programs. New vehicles such as the Specialized Centers of Research (SCOR) provided a means for integration of basic science and clinical research within grantee institutions. An important feature of this arrangement is that the entire program in lung diseases is responsible to a single administrative structure (the Director of the Institute through the Director of the

Division of Lung Diseases) and a single advisory structure (the Pulmonary Diseases Advisory Committee and the Institute Council). This provides coordinated and rapidly adaptable oversight of all interrelated programatic elements. It allows for continual adjustment of the relative importance of each element in the basic and applied research "mix". Thus it is possible within this structure to take rapid advantage of emerging technologies and developments to promote opportunities for health development. For example, the Pulmonary Diseases Advisory Committee may note an important new basic science technique which has been developed in another field and which would have important applications in lung research; using the mechanism of the Request for Application (RFA) relevant scientists are encouraged to move their work in this direction. Alternatively, the same committee may recommend a multicenter clinical trial when basic research has uncovered a treatment modality which must be quickly but rigorously tested before widespread public availability and (equally important) to define limitations to prevent the overuse of the new modality.

It is important to note that this highly desirable flexibility which provides a structure that is poised to respond to new advances, has been severely limited in the past several years by two forces. The first is the Congressional practice of authorizing funding by number of grants as well as by dollars. Although this practice was initially advocated by the scientific community and supported by NIH administrations as a means of providing a "floor" for project funding, it has served to severely limit the ability of Institutes to respond to new opportunities in these recent years of decreasing dollars and increasing costs of individual research projects. The second is budget decreases mandated by Gramm-Rudman-Hollings. The requirement for equivalent decreases in each program of the Institutes' portfolio hampers flexibility--in many ways, the major justification for a large multi-faceted bureau.

In general, the existence of multiple agencies involved in the conduct of and extramural funding for lung research has a favorable impact. Each agency has a unique orientation and mission. The overlapping interests and approaches function to ensure coverage of most important research areas and maintain a balance of activity. There is, we believe, very little duplicative funding of research. However, the agencies, on occasion, work at cross purposes and leave gaps in the total research effort. A good example is tuberculosis. No longer a major cause of death in the United States, it nevertheless remains a persistent and costly public health problem recently rising in incidence, due perhaps to high infection rates in certain groups of illegal aliens and patients at risk for AIDS. For the past two to three decades, no agency has regarded the control of tuberculosis as a significant part of its mission. As a result, cumbersome diagnostic and therapeutic techniques developed two generations ago are still used.

The ALA has long advocated the development of a strong mechanism for interagency cooperation in the broad field of prevention and control of lung diseases. We were most gratified when (after some delay) the Interagency Technical Committee on Lung Diseases was established under the Chair of the Director of the Division of Lung Diseases, NHLBI and the initial meeting identified several areas for important cooperative efforts. The ALA believes that such a mechanism, especially when tied to input from the general scientific and voluntary health agency sectors [i.e., when kept an "open" process], can be extremely effective in promoting coordination of efforts between federal research agencies with overlapping interests.

B. Setting of Research Priorities

In a pluralistic society priorities for the expenditure of public funds are always set in a complicated way, involving various elements of the political process as well as technical expertise. Research funding is no exception; priorities are set by Congressional action, the executive branch, and by agency management with varying degrees of input from advisory committees.

In biomedical research the NIH model, i.e. strong reliance on input from advisory committees with both expert and public representation, seems to be the most successful. The setting of priorities must always be linked to the state of scientific development, a determination which requires technical expertise. It does little good to set as a high priority the rapid conquest of cancer through clinical research when basic scientific advances are not sufficient to allow meaningful development of new therapeutic approaches. Careful structuring of advisory committees with open deliberations scrutinized by the interested public should be sufficient to avoid perpetuation of narrow self-interest by entrenched scientific groups.

C. Selection of Projects for Funding

Two models exist, that of professional management (best exemplified by DoD) and virtually complete control by the peer review process (best exemplified by NIH). The National Science Foundation system falls somewhere between these two. The advantage of professional management is tight control and may work best when specific research goals can be defined with great precision. The rigorous peer review system has several advantages. Foremost is the ability to call upon the judgment of the best scientists in a given field who are most likely to perceive creativity and merit in new departures. An additional advantage is the ability to structure peer review committees with balanced points of view and the resulting intrinsic "openness" of the meeting process of a peer review committee. The most often raised objection to the peer review committee system is that it tends to perpetuate the science done by well entrenched groups and schools of thought. Procedures are already in place, however, to limit this possibility. Continued efforts must be made to ensure broad representation of regional, institutional and scientific disciplines on review committees. Additional valuable procedures would be to limit terms to three years [NIH presently has four year terms] and allow NIH institutes to play a greater role in the appointment of the DRG peer review groups. The latter would provide for more rapid recognition of relevant new scientific fields and diminish the tendency of the NIH DRG study sections to self perpetuate.

2. Evaluation of Research Benefits

A. Strategies for Improving Health

The clearest biomedical research message of the modern era is that no single strategy will suffice to control disease. It was basic research on cellular mechanisms which led to conquest of many infectious diseases with subsequent development of vaccines for prevention and antibiotics for cure of these diseases. On the other hand, it is estimated that 350,000 deaths each year in the U.S. may be attributed to cigarette smoking. It was epidemiology, an applied science, which led to this discovery and which will be responsible for salvaging a substantial number of lives if preventive efforts toward the cessation of smoking are successful.

Each of these two scientific modalities, the one directed toward understanding basic cellular mechanisms of disease, the other toward understanding causation by the epidemiologic approach, have led to discoveries of potentially cost effective approaches to health promotion. The role of highly technical applied scientific approaches is more problematic. Sophisticated and expensive modalities such as cancer chemotherapy, renal dialysis and organ transplantation do not reduce mortality rates but frequently increase survival time. The quality of life during prolonged survival is often debated.

The "lung community" has in general avoided major involvement in these expensive, technical, applied science approaches toward the control of lung diseases. At the risk of oversimplifying a complex issue, ALA suggests that the responsibility for conquest of disease be placed with the sciences designed to understand basic disease mechanisms and let responsibility for cost effectiveness rest with those sciences which develop and improve preventive strategies.

B. Evaluation of Basic Research

It is likely that the scientific community is in complete agreement on basic research evaluation. Basic science should be evaluated by the peer review process; the only question should be "is it good science?" That is, have important new facts been discovered about living organisms? There are few ways to predict which basic science discoveries will be put to rapid use. Thus, the federal government must adopt a stance which is distinct from the industrial point of view.

C. Industrial Development

The biotechnology industry in the U.S. has become highly competitive and aggressive. It is felt that basic science advances which have commercial potential are being rapidly incorporated into the research portfolio of the private sector. One exception lies in areas where the public health impact may be substantial but the potential financial reward is poor, either because of limited market or potential product liability problems. A recent example lies in the area of vaccines for childhood illnesses. Federal support for production of highly selected "orphan" drugs or biological agents merits consideration.

3. Future Directions

The biomedical research enterprise in the United States is an outstanding example of the success which can be achieved by federal agencies when they are at their best. In a relatively brief period this country has become the undisputed leader in biomedical research. Major gains have been made in the control of a variety of diseases but it is important to recognize that these advances will surely be dwarfed by discoveries which are bound to follow in one or two decades. Advances in biotechnology, cell biology, and molecular genetics have brought us to the threshold of a virtual explosion in practical application of biomedical science. Therefore, this is not an appropriate time for a major overhaul of the federal support structure of biomedical research. In the view of most members of the scientific community, the system seems to be working well with major "payoffs" close at hand.

To summarize:

- The peer review process is essential to the success of the enterprise and should be strengthened.
- Development of research policy must be a joint effort between scientists and the public since policy cannot be developed without technical expertise.
- Major emphasis must continue to be on sciences designed to uncover basic disease mechanisms and on sciences designed to enhance preventive efforts. Expensive, halfway technologies of limited therapeutic potential must be carefully scrutinized prior to commitment of funds for their development.

- Opportunities continually present themselves in unexpected ways at unexpected times. It is essential to maximize the flexibility of agencies so that advantage may be taken of new opportunities as they arise and so that the "mix" of various research portfolios can be continually tuned to prevalent scientific and societal needs.

- The present system of multiagency funding for research in similar areas provides a distinct advantage as each agency approaches the problem with a different viewpoint and mission. However, there is the potential for working at cross purposes and omitting important elements of the overall mission. For this reason, establishment of interagency coordination by means of working committees with significant scientific and public input would be desirable in a number of disciplines.

STATEMENT OF DR. ROBERT W. KRAUSS

EXECUTIVE DIRECTOR

FEDERATION OF AMERICAN SOCIETIES FOR
EXPERIMENTAL BIOLOGY

for the

HOUSE COMMITTEE
ON
SCIENCE AND TECHNOLOGY

"FEDERAL POLICIES FOR BIOMEDICAL RESEARCH"

JUNE 6, 1986

I am Robert W. Krauss, Executive Director of the Federation of American Societies for Experimental Biology (FASEB). I want to thank you for the opportunity to submit a statement on FASEB's position concerning federal policies on biomedical research. I congratulate Chairman Fuqua and the members of the Committee for their strong support of scientific research.

FASEB is a nonprofit organization whose purpose is to develop and disseminate new knowledge in the life sciences through its meetings and publications. Its 28,000 members in seven constituent societies work in research, educational, and clinical centers across the United States. Since its founding in 1912, the Federation has counted 108 Nobel Laureates among its membership.

FASEB recognizes that federal support of research has been largely responsible for the United States' ability to remain in the forefront of biomedical and biological research worldwide. However, proposed cuts in this nation's R&D investment threaten America's world leadership. Both West Germany and Japan already outpace the United States in their percentage of GNP devoted to civilian research and development. According to the National Science Foundation, the 1985 R&D/GNP ratio for both West Germany and Japan was 2.6 percent; for the United States, 1.9.

Humanitarian benefits--the relief of disease and suffering, both in the United States and around the world--are the most important result of biomedical and biological investigations. Research also nourishes our economy. For example, it is estimated that medical research discoveries now used in nonhealth-related products contribute over $40 billion annually to the GNP. In addition, studies show that every dollar invested in medical research yields a $13 rate of return. Furthermore, biotechnology, a spin-off of NIH-supported research, offers the possibility of tremendous industrial advances with new techniques to clean up polluted waters, grow crops that resist disease and drought, and cheaply manufacture vaccines against livestock diseases.

How can Congress protect the United States' position as a research leader and assure that the results of new knowledge continue to fuel our economy? The solution rests heavily on a stable base of federal funding that allows scientists to plan the long-term basic research needed to solve the great mysteries of biology. The funding cuts at NIH in recent years have created a climate of uncertainty that prevents scientists from starting lengthy projects they may never be able to finish. This raises the legitimate question: why work for years trying to unlock the secrets of molecular genetics, brain biochemistry, immune responsiveness, or endocrine function when political decisions on funding may cause a sudden loss of research funds that may block the final solution to the problem? Congress must continue to recognize that long-term projects, while they may not yield immediate payoffs, provide the greatest hope for ultimately improving the health and welfare of mankind and reducing the nation's staggering medical bill, now totaling more than $400 billion a year.

Congress must also realize that the acquisition of new knowledge relies partly on a momentum that can be lost when federal funding dips unexpectedly. And when the momentum is lost in one area, ripples are felt in other life sciences disciplines, which increasingly rely on one another for sparks of intuition that can ignite new discoveries throughout biology. The problem involves more than lost momentum. Sudden funding gaps can cause research teams to be disbanded. Putting those teams back together and restarting research projects when funds are again available is costly. FASEB believes that the on-again, off-again approach to funding damages science, drives reputable investigators from the field, and, most importantly, discourages young people from entering research. We need a reliable financial commitment by the federal government, not merely for a year or two, but over the long haul.

Congress can also protect the United States' research superiority by funding a significant number of new and competing NIH grants. Through the efforts of FASEB and other groups, enlisting the cooperation of Congress, we were able last year to increase NIH research project grants from 5,000 to 6,100. We should maintain no less than the 6,100 grant level in FY87. These investigator-initiated grants provide the keystone of the NIH effort, exploring questions on the cutting edge of research and offering the greatest hope for progress against disease. Presently, only about 32 percent of approved grants are receiving funds. As a result, high quality research is being lost because of funding limitations.

Funding investigator-initiated research also ensures program flexibility. In its budget recommendations for FY87, the Ad Hoc Group for Medical Research Funding, a coalition of more than 150 organizations, including FASEB, comments, "Scientific activity continually identifies the next attainable horizon, as research proceeds from one discovery to another. The focus of support should be on talent and creativity rather than rigid priorities and precise directions, which must always be limited to what is already known."

Along with stable, reliable funding for investigator-initiated research, the progress of scientific knowledge and the momentum of discoveries depends on our ability to recruit and train the next generation of scientists. Unfortunately, Administration budgets for NIH and ADAMHA tell our bright, inquisitive undergraduate and graduate students, our young, promising scientists, and our established investigators that a career in federally sponsored basic biological research may be precarious at best. This instability also discourages promising young people from entering science and drives out the seasoned investigators needed to train new researchers. We are in the midst of an explosion of research opportunities in the biomedical sciences. In order to provide the steady infusion of talent necessary to exploit those opportunities, FASEB endorses recommendations that the federal government support at least 11,000 to 12,000 research trainees a year.

In addition, FASEB recognizes the value of the peer review system. By relying on experts working in the fields covered in grant proposals, peer review provides the best opportunity for creative thinking to be recognized, innovative research approaches to be exploited, and novel scientific areas to be unveiled. FASEB believes that peer review is still our best assurance that quality research is funded.

What more needs to be done? Of utmost importance is the modernization of research facilities in our nation's colleges and universities. Many of these facilities are now obsolete, and entirely new laboratories and equipment are needed for the high-tech research American scientists must conduct if they are to keep pace with competitors abroad. FASEB agrees with the underlying intent of HR 2823, the "University Research Facilities Revitalization Act," sponsored by Chairman Fuqua and others, which aims to renew the nation's deteriorating research infrastructure. But the Federation is concerned that the bill's provision setting aside 10 percent of the research money for facility improvement will reduce flexibility and erode funding for basic research, and should be dropped.

Furthermore, FASEB believes that a way must be found to reduce the amount of research money used to cover overhead. These indirect costs are important, and even some administrative costs must be recovered, but indirect costs cannot be permitted to rise indefinitely while the funds available for direct research costs decline. In return for cutting indirect costs, federal requirements for time and effort reporting and cost sharing should be eliminated.

Finally, FASEB is concerned that the vital importance of animals in biomedical and biological research be recognized at the same time provisions are made for the humane treatment of research animals. Without laboratory animals, many of our most important biomedical advances would not have been achieved. Many diabetics today owe their lives to animals used in insulin research. Thanks to research with animals, polio is no longer the major crippler and killer it once was. Feline leukemia, a highly contagious and fatal cancer in cats, can now be prevented, because of animal experiments. The list of vaccines, medicines, treatments, and basic knowledge derived from animal research is unparalleled in the history of science.

To help accomplish the goals FASEB believes Congress must pursue, the Federation recommends a fiscal 1987 funding level for NIH of $6.079 billion—an increase of about $86 million or 1.4 percent over a current services budget. This would include between $3.4 billion and $3.6 billion for NIH competing and noncompeting research project grants, a level sufficient to fund 6100 new and competing NIH grants in fiscal 1987. We also recommend a funding level of $465 million for research and training under the Alcohol, Drug Abuse and Mental Health Administration. And we support the Administration's request for $1.7 billion for the National Science Foundation, a 13.2 percent increase.

FASEB hopes that Congress will continue its enlightened investment in biomedical and biological research. The return we will all enjoy is better health for our people and for others around the world, increased productivity, and American leadership in life sciences research.

APPENDIX 2

FDA Orphan Products Grants FY 83 - FY 85

Drug/ Device	Project Dollars	Date of Award	Projected Date of Completion	Disease/ Condition
Phenytoin	219,104	9/30/83	8/31/86	Recessive dystrophic epidermylosis bullosa
WR 2721	60,575	9/30/83	8/31/84	Cystinuria
Pantethine/ Phosphocysteamine	66,952	9/30/83	8/31/85	Nephropathic cystinosis
^{131}I-MIBG	129,000	9/30/83	8/31/86	Pheochromocytoma
MESNA	99,873	9/30/83	8/31/87	Cyclophosphamide urotoxicity
Imipramine	82,341	9/30/83	6/30/87	Prepubertal depression
Fenfluramine	102,398	9/30/83	10/31/85	Autism
Harmaline	22,350	9/30/83	3/31/85	Cerebellar disorders
Chlorambucil	182,239	11/15/83	3/31/86	Progressive systemic sclerosis
VIL	126,156	11/15/83	10/31/86	Phenylketonuria
Carbonyl Iron	175,493	3/15/84	12/31/87	Iron deficiency anemia
DMPS	120,601	11/15/83	8/31/87	Childhood lead poisoning
Enzyme reactors	83,659	9/28/84	8/31/86	Phenylketonuria
Suppressin A	303,254	9/28/84	8/31/87	Histiocytosis X
CMV Vaccine	294,778	9/28/84	8/31/87	Prevent cytomegalovirus infection in renal transplant patients
Methotrexate	350,284	9/28/84	8/31/87	Juvenile rheumatoid arthritis
Teflon	34,043	9/28/84	9/30/86	Palatal insufficiency
Bacitracin	70,000	9/28/84	8/31/86	Pseudomembranous enterocolitis
Capsaicin	85,700	9/28/84	8/31/86	Post-herpetic neuralgia
Nafarelin acetate	87,443	9/30/85	12/31/88	Pubertal disorders
Thymosin	225,421	9/30/85	8/31/88	Chronic active hepatitis B
NP-59	129,095	9/30/85	8/31/87	Cushing's syndrome

FDA Orphan Products Grants FY 83 - FY 85

Drug/ Device	Project Dollars	Date of Award	Projected Date of Completion	Disease/ Condition
Cronassial	150,759	9/30/85	12/31/87	Charcot-Marie-Tooth disease
Ritodrine	54,530	9/30/85	12/31/88	Preterm labor
Deferoxamine	179,574	9/30/85	12/31/87	Iron overload in renal dialysis patients
Gammhydroxybutyrate	76,168	9/16/85	8/31/87	Narcolepsy
Dapsone	116,981	9/30/85	8/31/87	Pneumocystis carinii pneumonia
4-Methylpyrazole	65,991	9/30/85	8/31/87	Methanol poisoning
Tryptophan	149,783	9/30/85	9/30/87	Alcohol-related insomnia
L-carnitine	74,927	9/30/85	8/31/87	Carnitine deficiency in children on dialysis
Human surfactant	430,963	9/30/85	8/31/88	Neonatal respiratory distress syndrome
Fansidar	112,540	9/30/85	8/31/87	Pneumocystis carinii pneumonia
5-Hydroxytryptophan	241,975	9/30/85	8/31/88	Depression
Phenergan	130,931	9/30/85	8/31/87	Sickle cell anemia
Nitrazepam	65,210	9/30/85	8/31/87	Myoclonic seizures
Quinacrine	125,775	9/30/85	9/30/87	Pneumothorax in cystic fibrosis
Q fever vaccine	276,569	8/30/85	8/31/88	Q fever
Lithium and Phenytoin	289,851	9/30/85	3/31/88	Episodic violence

Wang 2118C

PROGRAM MANAGEMENT SYSTEM PROJECTS

- FOOD SAFETY
  - Chemical Contaminants & Pesticides
  - Food Additives
  - Food Sanitation and Quality Control
  - Food Service, Shellfish, & Milk Safety
  - Interstate Travel
  - Nutrition & Nutritional Labeling

- FOOD ECONOMICS
  - Food Labeling

- COSMETICS
  - Cosmetics

- HUMAN DRUGS
  - Antibiotic & Insulin Certification
  - Biopharmaceutics
  - Drug Abuse Treatment Monitoring
  - Drug Efficacy Study Implementation (DESI) Generic Drug Evaluation
  - Drug Experience & Trends Analysis
  - Drug Quality Assurance
  - Generic Drug Standards
  - Human Drugs: Bioresearch Monitoring
  - New Drug Evaluation
  - OTC Drug Evaluation
  - Poison Control
  - Prescription Drug Advertising
  - Prescription Drug Labeling

- NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH
  - National Center for Toxicological Research

- ANIMAL DRUGS AND FEEDS
  - Animal Drugs: Bioresearch Monitoring
  - New Animal Drug Evaluation
  - Animal Feed Safety
  - Safety of Animal-Derived Human foods
  - Monitoring Marketed Animal Drugs

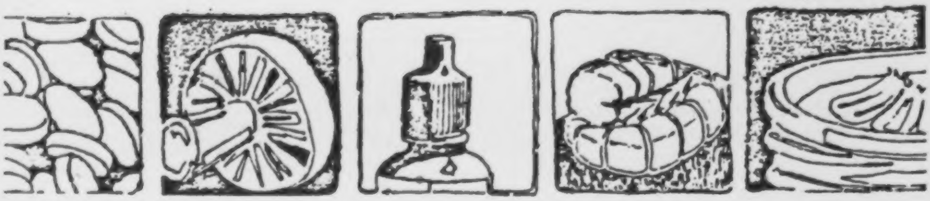
- RADIOLOGICAL HEALTH
  - Ionizing Radiation-Medical
  - Ionizing Radiation-Consumer and Industrial
  - Light Radiation
  - RF Microwave
  - Sonic Radiation

- BIOLOGICS
  - Bacterial & Allergenic Products
  - Biologics: Bioresearch Monitoring
  - Biologics Safety, Efficacy and Labeling Study
  - Blood and Blood Products
  - Virial & Rickettsial Products

- MEDICAL DEVICES
  - Investigational Device Exemption Activities
  - Medical Device Monitoring & Quality Assurance
  - Medical Device Premarket Approval Activities
  - Medical Device Standards Activities

FDA's Scientific Innovations: An Inventory of Their Uses by Industry, Academia, Health Care Providers, and Other Government Agencies

An OPE Study



NOTE

The Office of Planning and Evaluation, OC, produces numerous studies for publication each year. Some embody the results of a major research project undertaken by OPE and are intended to be an authoritative contribution to the field.

Others are less-formal documents and are therefore less comprehensive in scope. They may be the result of smaller and more narrowly defined research projects or they may be supporting technical papers prepared in connnection with a major project.

Often such papers present the work of one or more authors. The manuscripts are subject to review comparable to that for publication in a professional journal.

Previously published studies: (Partial list)

An Analysis of Prescription Drug Recall Rates. OPE Study 52, April 1980.

FDA Measures of Drug Quality. OPE Study 63, January 1983.

New Animal Drug Applications: An analysis of Approval Rates, Times, and Deficiencies from 1972 through 1981. OPE Study 65, May 1983.

New Drug Introductions, Discontinuations, and Safety Issues in the United States and the United Kingdom 1960-1982. OPE Study 68, January 1984

Compliance with Current Good Manufacturing Practices Regulations and Selected Characteristics of Drug Manufacturers. OPE Study 71, January 1985.

The innovations within these groups have been detailed in three tables. Each innovation is described in terms of the problem it addresses, the nature of the innovative solution, and the impact of the innovation outside FDA.

Hazard Determination

Table 1 contains 14 examples of innovative contributions made by FDA researchers to the science of hazard determination. In some cases the product itself represents the innovation; in other cases the product is incidental to the new scientific knowledge contributed. The innovations range from fairly simple adaptations of test equipment that allow new precision or accuracy, to the development of complex systems that integrate electronic data processing with sophisticated scientific principles. The disciplines represented range from toxicology to analytical chemistry and cell biology.

Approximately two-thirds of the examples in this table involve laboratory methodology. More than half of all the examples involve food safety and nutrition. In about half of the projects cited, new information was generated that changed the viewpoint of the scientific community about a chemical, physical, or biological phenomenon; the remaining half are improvements on known principles that have subsequently been applied outside FDA. Chart 1 shows the distribution of products and processes involved in hazard determination.

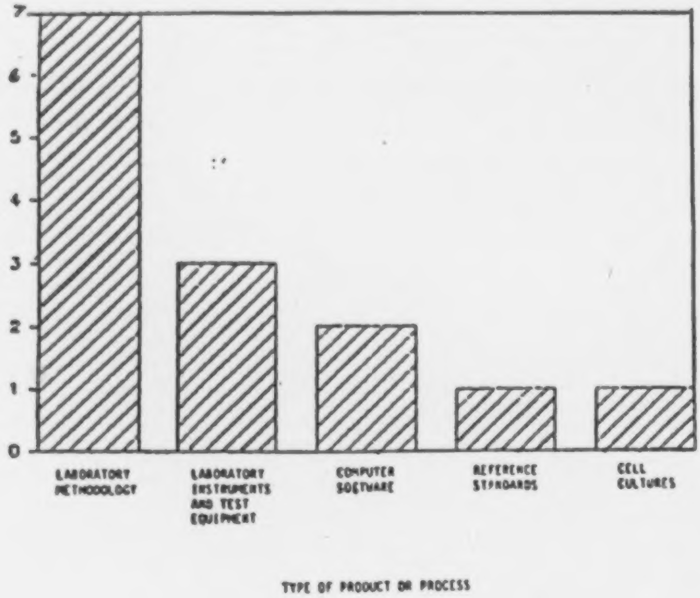


CHART 1: NUMBER OF EACH TYPE OF PRODUCT OR PROCESS IN HAZARD DETERMINATION

Table 1

HAZARD DETERMINATION INNOVATIONS

	Problem	Solution	Impact Outside FDA
1.	Standard methods to measure drug dissolution rates were needed.	Drug Dissolution Testing FDA developed and taught methods to measure drug dissolution.	These methods are used world-wide.
2.	A modern set of toxicological procedures was needed to assess the biological effects of food and color additives.	Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Foods ("The Red Book") FDA has experience in analyzing food toxicology data that cannot be found elsewhere. FDA scientists put together a clear, concise description of the data requirements to evaluate the chronic, subchronic, carcinogenic, and second-generation effects of chemicals.	The number of tests done that do not contribute additional knowledge or generate misinformation, was reduced. "Represents a significant contribution to science and to orderly, efficient regulation"--Grocery Manufacturers of America.
3.	The USP method for testing membrane filtration sterility needed improvement.	Membrane Filter Cutter FDA developed a cutter to cut the membrane into two halves so that the same amount of product could be cultured in two different bacteriological media.	Many biological and pharmaceutical manufacturers adopted the equipment design for routine use in sterility testing.

Table 1

HAZARD DETERMINATION INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
4. A method was needed to measure possible genetic effects of food chemicals.	Heritable Transformation Test FDA adapted the methods used by Oak Ridge Laboratory to study mouse genetics to test food chemcials.	The method developed is now used by industry and EPA.
5. A process was needed so that information submitted to FDA or obtained by FDA researchers about the biological effects of food chemicals, the uses of food chemicals, the amount of public exposure to certain chemicals, and other data could be used for assessing food safety as well as for planning additional studies.	Priority-Based Assessment of Food Additives (PBAFA) FDA has developed a computer-based encyclopedia of data for food additive research including amounts used, the types of foods in which additives are used, and current research data. FDA developed PBAFA to provide a logical priority system to identify research needs necessary to assess food additive safety.	The system reduces the food industry's uncertainty about costs in food and food package decisions. For example, if a firm wants to use compound "x" in a new food process, the system tells what needs to be done to assess the safety of its use. Trade secret data are isolated so that industry can access this system directly.
6. A method was needed to test whether chemicals are transformed into mutagens by metabolic processes.	Host Mediated Assay FDA demonstrated that the microorganism Salmonella typhimurium could be exposed to metabolites by injecting these organisms into the abdominal cavity of mice that have been fed chemicals.	The method developed is widely used today by scientists in this field.

Table 1

HAZARD DETERMINATION INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
7. Research was needed to determine what the effects of certain chemicals are on fetal development.	Second Generation Studies in Rodents FDA developed a toxicology protocol for second generation studies.	Studies showed that the placenta does not exclude foreign substances (xenobiotics) from developing fetuses. This changed the thinking of the scientific community.
8. Biological reduction of azo dyes can produce mutagenic aromatic amines. A method was needed to evaluate azo dyes for their potential to be metabolized into mutagens.	Modified Ames Test FDA scientists adapted the Ames test that uses micro-organisms to detect mutagenicity. Five distinct modifications were developed to optimize the test's ability to detect mutagenic reduction products.	This test is used by dye manufacturers to establish product safety.
9. Multiple trials that use many animals to assess genetic effects generate great quantities of data, which are difficult to analyze.	Adapt ADP to Toxicology FDA scientists worked to develop decision rules and software to analyze data from multi-animal toxicology studies.	The software developed is now used by industrial laboratories.
10. Accurate measurement devices were needed to begin studies to determine the effects of low-level diagnostic ultrasound on the fetus.	Diagnostic Ultrasound Meter FDA scientists were aware of theoretical work done on measuring ultrasound. FDA bought and tested instruments based on this model.	The device is now being marketed for use by UMA, Inc., and is used by health care providers. Source: (38)

Table 1

HAZARD DETERMINATION INNOVATIONS
(continued)

PROBLEM	SOLUTION	IMPACT OUTSIDE FDA
11. Many scientists use statistical software packages such as the Statistical Analysis System (SAS), but SAS does not perform every analysis necessary in toxicology studies.	Computer Statistical Procedure: PROC CHRONIC FDA scientists developed a SAS procedure for chronic toxicological uses, PROC CHRONIC.	The procedure has been submitted for inclusion in the SAS supplemental library. Many toxicologists are already using it.
12. The limulus amebocyte lysate (LAL) test provides an *in vitro* alternative to the standard rabbit pyrogenicity test for bacterial endotoxins. Reference reagents for the control of the LAL test were needed.	National Reference Endotoxin FDA collaborated in the preparation of a large supply of purified bacterial endotoxins.	The endotoxin, designated EC, has been used to produce a series of lots of Reference Standard Endotoxin which is used by all lysate manufacturers licensed by FDA and by the USP. The same endotoxin is currently being integrated into an international reference preparation by the World Health Organization.
13. There was a need to achieve uniform conditions for the freeze-drying of biological substances.	Direct Contact Tray for Freeze Drying FDA scientists developed a tray assembly for vials or ampoules that maintains direct and constant contact between the bottom of each container and the shelf of the freeze-drying apparatus.	The equipment manufacturers have used the principles of the design changes to achieve uniform freeze-drying of biological substances.

Table 1

HAZARD DETERMINATION INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
14. There was a need to develop a simple biological screen to evaluate the toxicity or biological potency of mixtures in the food supply that were suspected of containing halogenated congeners of the dibenzo-p-doxin, diberzofuran, and biphenyl classes of chemicals, without having to test all possible combinations. The number of possible congeners exceeds 400, and chemical analysis of mixtures cannot distinguish toxic from nontoxic components.	*In Vitro Testing Using a Rat Hepatoma Cell Line* FDA used cultured rat hepatoma cells to detect the relative potency of a mixture against a standard response produced by the most toxic and biologically potent chemical in these classes: 2,3,7,8-tetra-chlorodibenzo-p-dioxin (TCDD). This *in vitro* screen was developed to single out the most reactive mixtures for identification of specific compounds by chemical means. This made possible the precise quantification of toxicant responses in the rat hepatoma bioassay system and the standardization of the methodology by rigorous statistical treatment of data. FDA introduced the concept of TCDD equivalents to evaluate the biological potency of mixtures and applied this method to screen gelatins, rice oil, and fish samples.	FDA has made this cell line available to other government agencies, industry, and academia through distribution by the American Type Culture Collection as a certified cell line, ATCC CCL 1548. Reference to the method developed at FDA appears in more than 100 documents and publications. Research at Texas A&M University has further expanded the use of this bioassay by testing 80 additional purified congeners, introducing other indices of cytotoxicity, validating the *in vitro* response against *in vitro* parameters of toxicity, and applying the test to screen incinerator waste.

Hazard Control

Table 2 contains 34 examples of FDA's innovative contributions to the technology of hazard control. These products range from "how to" information and computer software to sophisticated instruments. FDA is responsible for many innovations in laboratory tests used to prevent hazardous products from being distributed commercially, and the agency also develops and maintains authentic or reference samples that are used by industry quality control laboratories.

More than one-third of the examples in Table 2 are related to medical devices and radiation. Another one-third are food related. The other examples are equally divided between drug and veterinarian products. Of the six kinds of products involved in hazard control, the largest proportion--more than one-third--are instruments and test equipment. The second most frequent kind of product is test methodology. More than one-fifth of the total are control methodologies and procedures that can be applied to prevent malfunctions or contaminations that result in hazardous products. Chart 2 shows the distribution of these types of products and processes.

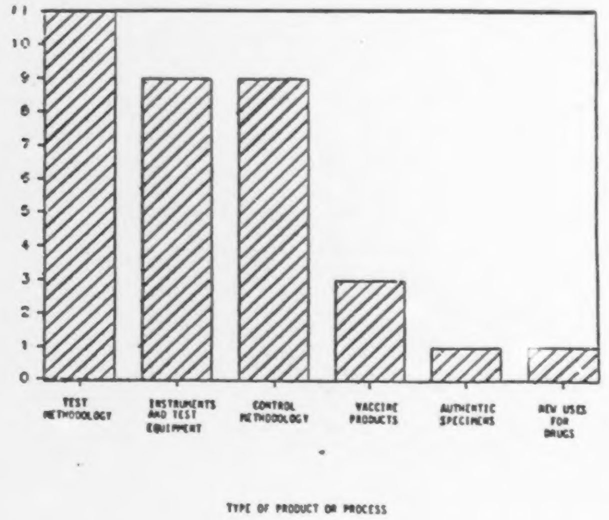


CHART 2: NUMBER OF EACH TYPE OF PRODUCT OR PROCESS IN HAZARD CONTROL

Table 2

HAZARD CONTROL INNOVATIONS

	Problem	Solution	Impact Outside FDA
1.	A means was needed to measure the amount of radiation to which a patient is exposed without actually exposing the patient to the radiation.	Lucal Chest Phantom FDA developed a "phantom," using lucite and aluminum, which estimates the exposure received by a typical patient.	Industry is receptive to the concept and the product is currently being used in a nationwide study. It is commercially available from two sources.
2.	The quality assurance methods and instruments used by many firms in the canning industry were outdated and tolerated a small rate of spoilage.	Critical Control Point Sterilization FDA developed the approach of monitoring the critical parameters of food sterilization. This technique results in more reliable and reproducible results.	In cooperation with the National Food Processors Association, FDA has conducted more than 100 seminars for industry people in critical-control-point methods for canning sterilization and container integrity assurance.
3.	State and local sanitation programs needed an affordable and more efficient means of processing data on kinds of establishments, types and frequency of problems, and other relevant factors.	Sanitation Program Information Formulator ("SPIF") FDA and FDA contractors developed.the SPIF system, which contains three programs: report generation, file maintenance, and mailing.	Software, available through Opportunity Systems, Inc., is being adopted nationwide.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

	Problem	Solution	Impact Outside FDA
4.	Standard methods to test pacemakers for leaks by using helium are unreliable because helium is absorbed by polymers used to encase the electronic circuit.	Optical Correlation to Measure Leak Rates in Sealed Packages This method does not use a tracer gas and is therefore unaffected by polymeric absorption and remission. The method is also accurate over a wider range of leak rates. A patent application has been filed.	No instrument is yet available, but various industries are looking into developing their own instruments for quality control purposes.
5.	A nondestructive test was needed to evaluate wear on implant surfaces.	Holographic Microtypography Analysis FDA scientists developed many applications of holographs to the analysis of medical devices.	Orthopedic implant manufacturers are exploring the use of this technology on articulative prosthetic surfaces (knees, hips, etc.)
6.	A method was needed to determine whether color television sets might pose a hazard by emitting x-rays at significant levels. Available x-ray meters were "point source" detectors and thus could not be used to test the entire surface of a TV.	"Stoms" Meter An FDA scientist designed and patented a new meter that could obtain readings over a wide area.	FDA established that there was a risk of x-rays being emitted from color televisions and discovered that rectifiers could also emit radiation. The "Stoms" meter is still widely used in industry, but more sophisticated and more portable devices have now been developed.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
7. Sulfa compounds used to treat diseased swine are secondary carcinogens. A method was needed to detect sulfa residue in swine tissue to establish conditions for using this drug in food producing animals.	Thin Layer Chromatographic Detection of Sulfa Residues A method was developed under FDA contract using thin layer chromatography capable of identifying sulfa residue extracted from swine tissue.	This method was modified in an AOAC collaborative study and has been used by USDA and industry in the development of protocols for the use of drugs such as sulfamethazine by producers of food animals.
8. There was a need to develop a procedure for performing and evaluating the neurovirulence test for live attenuated poliovirus vaccines that provided a high degree of interlaboratory correlation while using fewer nonhuman primates.	New Monkey Neurovirulence Test Collaborative investigations undertaken by FDA and other U.S. scientists, the Biologics National Control Authorities of Canada, and by Britain over a period of 5 years has resulted in the development of a procedure with improved reliability and fewer primate subjects.	Virtually all producers and control authorities throughout the world are using the new procedure.
9. Industries composed primarily of small firms sometimes face quality control problems that are beyond their technological resources.	Food Processing and Packaging Technological Expertise FDA scientists have provided information, sampling techniques, and test equipment operation methods to eliminate hydrogen peroxide residues from sterilized equipment, etc., to numerous firms to help them overcome problems in food processing or aseptic food packaging.	Numerous firms have upgraded their quality control technology.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
10. Color additives can contain hazardous chemical contaminants or by-products. Methods and expertise were needed to improve the efficiency and effectiveness of food color quality control.	Color Technology FDA's contributions include computer-augmented high volume testing, the application of high-performance liquid chromatography, and applied expertise in identifying the substances causing chromatographic responses. FDA also provides reference standards and their spectra.	Information has been shared with industry to upgrade control technology as well as solve ad hoc problems.
11. There was a need for identification and quantification of mycotoxins in food products.	Silica-gel Plates Sensitive, rugged methods were developed based on thin layer chromatography, high performance liquid chromatography, and gas liquid chromatography.	These methods were used to develop human exposure data on the mycotoxins leading to current regulations and control programs.
12. An analytical method was needed to permit the practical surveillance of foods for pesticide residues--that is, a method capable of determining several pesticides in a single analysis.	Multiresidue Analysis FDA pioneered much of the development using paper, thin layer and later gas chromatography, and now high performance liquid chromatography, developing entire methodological schemes to systematically analyze for residues of many pesticides simultaneously.	This methodology has been widely used for many years by scientists in the field (including industry) and has contributed to the evolution of current methods that use the most advanced gas and liquid chromatographic techniques for widespread monitoring of foods for many pesticide residues.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
13. Methods were needed to extract, identify, and quantify filth contaminants in food products.	Microanalytical Methods FDA microanalytical specialists have developed or adapted procedures for extracting and quantifying filth contaminants, including rodent hair and excreta, insect fragments, and decomposition.	These methods have been made available in the microanalytical manuals. Thousands of these publications have been used worldwide. New developments have been published in FDA Technical Bulletins 1 and 2 available through GPO. Industry scientists have been trained in microanalytical methods to detect filth and decomposition.
14. A procedure was needed to detect minute amounts of a potent animal carcinogen, such as volatile N-nitrosamine.	Gas Liquid Chromatography-Thermal Energy Analyzer and Gas Liquid Chromatography-Mass Spectrometry FDA developed these methods for determining and confirming the identity of volatile N-nitrosamines. Very selective and sensitive methods were made available for the large scale screening of food products for toxic contaminants-which led to significant reductions in the levels, and suppression of a potential health hazard.	FDA trained industry scientists in these methods. These scientists were then able to identify problem areas in their processes and to make appropriate changes. As a result, potentially hazardous nitrosamines were significantly reduced or eliminated in consumer products such as bacon, beer, malt and malt beverages, whiskies, and rubber baby bottle nipples.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
15. A means was needed to use radiographic test equipment at specific sites in relation to x-ray equipment without exposing personnel running these tests to excessive x-ray exposure.	Radiographic Test Stand FDA designed, and in 1975 patented, the test stand to hold radiographic test equipment at specific positions relative to radiation sources. A private firm has been licensed to produce these stands.	More than over 500 of these stands are in use. States, local health organizations, and private firms use them.
16. Unnecessary patient exposure to x-rays was being caused by equipment that projected an x-ray beam larger than the film being used.	Automatic X-ray-Field-Size-Limiting System FDA scientists designed and demonstrated a system that automatically limits the x-ray field size to the dimensions of the film being used (collimation). This design was patented.	Automatic collimation is now routinely used in diagnostic radiology. General Electric has designed its own automatic collimator. Other firms use modifications of FDA's design. Automatic collimation is a standard feature of x-ray equipment sold commercially.
17. A portable instrument was needed to measure the intensity and duration of x-ray exposure.	Fast Charge Digitizer FDA scientists produced and patented the prototype key component. MDH Corporation produced the complete unit, partially supported by FDA contract.	More than over 2,000 of these units have been sold to state and local governments, hospitals, and clinics.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
18. FDA, states, other federal agencies, and some private firms needed authentic reference samples or information on laboratory methods to be able to test products for industrial chemical contaminants.	Industrial Chemical Respository FDA maintains a collection of reference materials and a computerized data base on analytical characteristics for significant industrial chemical contaminants.	Scientists outside FDA use this system 200 to 300 times per year.
19. Many agricultural commodity firms are small, and certain quality control tests require equipment that is too expensive for them to use.	Pulper Rock Counter A pulper is a device used to produce a homogeneous mixture of an agricultural product in order to be able to determine relative filth content. FDA developed prototype plastic slides to replace the much more expensive glass slides used in pulper rock counters for fruits and vegetables.	Pulpers with these slides are now commercially available and widely used.
20. Food animal producers and veterinarians needed up-to-date information on a variety of issues associated with hazard control technology.	"CVM Memos" and Educational Guides CVM memos are sent to producers, practitioners, state agencies, and extension services. FDA produced a comprehensive guide titled "Contamination of Animal Feed-Stuffs: Developing a Quality Assurance Program."	Industy has requested more than 1,000 copies of the education guide alone. The guide is also sent to trade associations and local agencies, reaching a large audience.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

	Problem	Solution	Impact Outside FDA
21.	Phantoms for testing the resolution and uniformity of nuclear medicine cameras require an internal radiation source. These sources are expensive, dangerous, and difficult to transport.	FDA Test Phantom FDA developed a test phantom made of lead and plastic that can be activated by radiopharmaceuticals on site. The new phantom is safe, cheap to produce, and easy to transport.	The test phantom is currently being produced commercially by Victoreen, Inc.
22.	Diathermy uses microwaves to induce therapeutic heating of muscle tissue. There was a need for a device that would uniformly focus microwave energy and reduce patient exposure from leakage.	Microwave Diathermy Applicator FDA scientists devised a prototype diathermy applicator that effectively focuses microwave energy.	This device is currently being manufactured under license by TAG MED.
23.	The only effective means of monitoring the effects of RF/microwave diathermy is a temperature sensor. Reliable sensors were needed that could be inserted into treated tissue with minimal trauma.	Miniature E-Field Probes FDA scientists established performance parameters and solicited ideas. A prototype device was ultimately developed under FDA contract. The probe is small, flexible, and easily inserted into treatment areas.	This device is currently being commercially produced by NARDA.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
24. Although the National Academy of Sciences recommended that shielding be used to reduce the exposure of reproductive cells to x-rays, shielding was infrequently used because there were few clinically acceptable and readily available shields. Also, x-ray technicians had a poor understanding of how and when to use the shields.	Gonad Shield An FDA contractor developed flat, contact, shadow, and shaped shields; FDA then made intensive efforts to educate technicians in their use.	These shields are now commercially available and have been purchased and used nationwide.
25. Doxorubicin, a wide-spectrum antibiotic used against cancerous tumors is cardiotoxic. Doxorubicin is used to treat a wide variety of neoplastic diseases. A major limitation to optimal use is dose-related chronic cardiotoxicity.	Drug Toxicity Attenuator FDA, in collaboration with the National Heart, Lung, and Blood Institute, discovered that the drug ICRF-187 reduces or prevents the cardiotoxic effects of Doxorubicin.	The impact of ICRF-187 on Doxorubicin cardiotoxicity in patients is now being evaluated in a clinical study at New York University. Veterinarians are also beginning to examine the potential benefical effects of this drug combination.
26. A company that produced human insulin from recombinant DNA had a problem with contamination from its *E. coli* parent cell line.	*E. coli* Contamination Control FDA suggested methods to detect and control *E. coli* polypeptide contamination in the insulin.	The manufacturer has adopted FDA's suggestions and has improved its product.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
30. Many questions have been raised in recent years about the effects of mycotoxins in feeds for food-producing animals. Knowledge of the distribution in nature of the toxin-producing organisms, as well as the storage, processing, and distribution methods that prevent or minimize toxin formation in grains was needed.	Mycotoxin Conferences FDA coordinated and partially funded reviews of the literature and sponsored scientific conferences to bring experts together. FDA recorded the proceedings of these conferences for dissemination among the scientific community. The proceedings are available through the National Technical Information Service.	Feeders of food producing animals use this information regularly.
31. A standardized diet was needed to enhance screening of the growth-promoting characteristics of antibacterial animal feeds. Pharmaceutical manufacturers needed a better way to evaluate the growth promotion characteristics of various antibacterial food additives.	Poly-galacturonic Acid in Rye-Based Diets FDA scientists discovered the agent in rye-based diets that allowed screening of anti-bacterial growth-promoting potential was poly-galacturonic acid (or pectin).	This and similar diets are widely used by pharmaceutical managers to evaluate the growth-promoting potential of antibacterial food additives, using fewer animals for shorter periods of time.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
27. There was a lack of standardized and well-characterized cell cultures for the production of biologics.	Standardized Vaccine Cell Line FDA developed and patented a cell line, DBS-FRHL-2, for the production of vaccine.	These cells were used for some rabies vaccines. The standardized approach FDA used induced others to develop cell lines that are still in use.
28. There was no vaccine for *Hemophilus influenzae*.	H Flu Vaccine Methodology FDA developed a method of coupling an H-flu polysaccaride with a tetanus toxoid to produce a vaccine that appears to elicit an effective immune response in infants.	Connaught Laboratories used this technique to develop its own H-flu vaccine, which NIH will field-test in Alaska.
29. There was no vaccine for rubella, nor was there a practical test for determining immunity to rubella suitable for routine use.	Rubella Vaccine and Serum Antibody Test FDA scientists developed and patented a serological test for rubella antibodies and an experimental vaccine strain.	The rubella immunity test is still being used. The vaccine strain was used by manufacturers to produce the first licensed rubella vaccines.

Table 2

HAZARD CONTROL INNOVATIONS
(continued)

Problem	Solution	Impact Outside FDA
32. The most common disease of breeder cattle is bovine pneumonia. A better method was needed to test the relative effectiveness of antibiotics used in cattle.	Adrenocorticotropic Hormone (ACTH) Stress Model FDA developed a method known as the ACTH stress model, which predisposes cattle to bovine pneumonia. This method allows reliable and uniform infection, greatly reducing the time of an effectiveness study.	This model is used to evaluate the effectiveness of antibiotics in cattle and should significantly reduce study costs.
33. To detect trace quantities of animal carcinogens such as residual monomers (vinyl chloride, vinylidene chloride, acrylonitrile, 1-3 butadiene, etc.) in polymeric food packaging materials.	Residual Monomer Detection FDA developed methods for determining and confirming the presence of these compounds or their toxic reaction products in polymeric packaging and their migration to foods.	Through training and cooperative efforts, FDA has promoted expertise in the industry so that industry scientists can monitor their own products. Industry now has a program for analyzing polymeric packaging so that residual monomer levels can be kept as low as technologically feasible, limiting migration of these toxic compounds to foods.
34. There was concern that widely used pelvimetry was exposing fetuses to radiation not justified by the medical utility of the procedure.	Pelvimetry Referral Criteria A FDA-sponsored study group worked closely with a private coalition of 16 teaching hospitals to obtain data on pelvimetry. Using this and other data, a panel drafted recommendations on pelvimetry referral criteria in January 1979.	These or similar criteria were accepted by the American College of Radiology and the American College of Obstetrics and Gynecology. A 1980-81 nation-wide study indicated that use of the panel's recommendations caused a 60% drop in the number of pelvimetry examinations in the hospitals that were studied.

Other Scientific Applications

Sometimes FDA possesses knowledge or equipment that proves useful to other scientific endeavors. Table 3 presents 8 examples of how FDA scientists have contributed their expertise to technological challenges apart from their work in hazard determination and control. While not innovations per se, these are examples of the use of unique FDA knowledge by non-FDA researchers to help solve some of society's problems. These indirect contributions can be viewed as spin-off benefits from FDA's scientific activities.

Table 3

OTHER SCIENTIFIC APPLICATIONS

	Problem	FDA's Contribution
1.	The Canadian government decided there was a need to regulate vomitoxin in grain. Good analytical methodology was lacking, however, making any attempts at regulation questionable.	FDA staff developed and tested an excellent procedure to survey foods and feeds for vomitoxin. The Canadian government is considering using this method. Also, the data generated were used to support the FDA advisory on vomitoxin in grains.
2.	The lack of timely access to radiology services is a major problem for millions of Americans in rural areas and for members of the armed forces that depend on small hospitals on military bases.	Teleradiology, the transmission of televised radiographic images over telephone lines, was developed at FDA with support from the Defense Department. Participants included several university centers; Army, Navy, Air Force, and public health radiologists; and engineering specialists from MITRE Corporation.

Table 3

OTHER SCIENTIFIC APPLICATIONS
(continued)

Problem	FDA's Contribution
3. A medical researcher at Johns Hopkins University needed to be able to quantify the vitamin C concentration in the aqueous humor of the eye.	FDA scientists are able to accurately determine the vitamin C concentration in very complex mixtures. FDA scientists provided their protocol to the investigator at John Hopkins.
4. Determining the vitamin C content of foods and food supplements was expensive and time consuming.	FDA scientists developed the basic fluorometric assay and helped develop the automated fluorometric method that is now widely used.
5. Medical research on ulcers requires understanding the release mechanism for hydrochloric acid and digestive enzymes in the stomach.	Research done in FDA in support of the visiting scientist program on helminth infections in animals developed a method to detect and accurately quantify small amounts of pepsinogen. This method is available for studies on the release mechanism for hydrochloric acid and enyzmes in the stomach.
6. Cardiac researchers at Johns Hopkins University needed an animal model to study diethylcarbamazine (DEC) shock syndrome.	FDA research developed an *in vitro* method for producing *Dirofilaria immitis*. Dogs infected with this parasite are subject to DEC shock syndrome.

Table 3

OTHER SCIENTIFIC APPLICATIONS
(continued)

Problem	FDA's Contribution
7. Rats used in toxicological studies often defecate and urinate in their food and later consume those wastes, thus consuming metabolites of test compounds and jeopardizing study results.	An FDA scientist developed the "Hunziker Feeder," which keeps the food clean. Hazleton Labs is interested in manufacturing the feeder.
8. There were no uniform standards for tissue typing.	FDA sponsored a workshop that established guidelines and uniform standards for the field. This standardization has led to the common use of tissue-typing techniques in paternity suits.

FDA SCIENTIST COMMUNICATION

EXECUTIVE SUMMARY

The study of FDA scientists and how they communicate was completed by the Office of Planning and Evaluation in response to an interest expressed by FDA management, particularly the Science Coordination Committee. The decision to proceed with the study was supported by the fact that good science has a central role in the effective functioning of FDA. As a situational analysis, the study concentrates on the present time. Historical information was elicited and used only to a very limited extent.

The study has two objectives:

1) To acquire a thorough profile of FDA scientists, and

2) To describe how FDA scientists communicate with others (inside and outside the agency) concerning technical matters and policy and program matters, and to ascertain the scientists' evaluation of the communication channels.

In April 1983, a questionnaire was distributed to FDA employees who were identified as scientists by their job classification series. All pay systems, such as SES and the PHS Commissioned Corps, were included, and all FDA installations where scientists are located were covered.

A demographic profile was constructed to satisfy the first objective. This profile is from two sources: the FDA personnel data base, and information gathered with the questionnaire.

FDA's personnel system identified 2,157 employees occupying 27 "scientific" job series. Some of the characteristics of these employees are:

- Job series--the largest group of scientists is chemists (43% of the total) followed by microbiologists (12.5%).
- Pay plan--66.7% are GS; 20.4% are Merit Pay; and 10.7% are Commissioned Corps.
- Age--the average age of FDA scientists is 44. (5% are under 30, whereas 48% of the comparable scientists in the national work force are under 30.)
- Sex--22% are female, which is comparable to the percentage of female scientists in the United States.
- Supervisory status--26% of the scientists are supervisors.

The questionnaire was distributed to the entire population of 2,157 scientists of whom 1,216 (56%) responded. The responses produced the following profile:

- Highest Level of Education--41% have baccalaureate degrees; 24% have master's degrees; 27% have Ph.D.s; 7% have M.D.s and 6% have other degrees.
- Education by Organization--The Center for Food Safety and Applied Nutrition has the highest proportion of Ph.D.s (41%); while the Center for Drugs and Biologics has the highest proportion of M.D.s (45%).
- Publications--24.4% of the scientists responding have published four or more times; while 50.5% of the respondents have had no publications in refereed journals in the last five years.
- Highest Publication Rates--Ph.D.s are the most highly published degree group; NCTR generated the most publications per scientist.

The survey included questions about how the respondents spend their time among four scientific activity categories:

Evaluation review--activities that require critical and systematic evaluation of scientific data for clearance or approval purposes.

Methods development--developing new or improved analytical methods for laboratory application or compliance testing.

Compliance testing--testing of products or materials to determine conformity with standards.

Hazard determination--laboratory studies, epidemiological investgations, and product surveys for the purpose of establishing risk or setting standards.

The respondents indicated that they spend their time on these activities as follows:

Total FDA scientist time:

Evaluation review	- 33%
Methods development	- 24%
Compliance testing	- 24%
Hazard determination	- 15%
Other activities	- 4%

SCIENTIST COMMUNICATION

In order to describe the scientist communication throughout FDA, three dimensions or characteristics of communication were selected. They are:

- Frequency;
- Direction; and
- Value

Frequency is how often a particular kind of communication takes place. Direction of communication answers the question of who gives and who gets information when communication takes place. For value, the respondents were asked to rate the usefulness of each exchange to them personally using a scale of 1 to 5, 1 being "not very useful" and 5 being "extremely useful." These three dimensions were considered separately for 1) scientists communicating on science matters and 2) scientists communicating on policy and program matters.

Science Communication

The most frequently used channel for science communication in FDA is one-to-one contact with others in the branch. The second most frequent is one-to-one with the supervisor. Both of these channels are used almost daily. Frequency of science communication in meetings within FDA is similar to one-to-one communication; it occurs more often within the branch than with more distant contacts. Communication outside of FDA concerning science, both one-to-one and in groups, averages between six and twelve times a year for the FDA scientist. The only exception is in communication with industry, where contacts occur nearly every two weeks. FDA scientists also report that they attend scientific professional society meetings about three times a year. They attend lectures, seminars, and other types of continuing education 16 times a year, and they consult the professional literature almost daily.

FDA scientists think it is more likely that they will give information than receive it when engaged in one-to-one communication about science inside FDA. FDA scientists give more information than they receive in one-to-one contacts outside their center and at meetings. They get information at the highest rate at meetings at the division level. In most cases, contacts outside FDA by scientists result in their giving information, particularly when other governments are involved. However, when the contact is with academia the FDA scientist gets information slightly more than half of the time.

All the science communication channels that FDA scientists use have a moderate to high value. Inside FDA one-to-one communication with others in the branch was rated as the most valuable channel. It was followed closely by one-to-one communication with the supervisor. Outside FDA, higher value was attached to science communication with individuals and organizations outside of the federal government in comparison with channels involving other federal agencies. Contact with academia was valued most highly among the non-federal channels. The "non-interactive" type of communication, such as professional meetings and literature, was valued highest when compared with other communication. The scientists also got the opportunity to suggest improvements. All of the channels were selected for improvement by at least one respondent, but 35% of those answering this question named "professional society meetings." Follow-up interviews indicate that this means the scientists want to be able to attend more meetings.

Policy and Program Communication

The most frequently used channel for policy and program communication in FDA is one-to-one contact with supervisors, occurring more than twice a week. Among the other one-to-one channels inside FDA, "with others in the branch" is the second most frequently used, at just under twice a week. Meetings are used less frequently than one-to-one contacts for policy communication. Meetings within the branch occur two or three times a month. Meetings at the division level are held less than twice a month, and meetings elsewhere in FDA happen less than once a month for the individual scientists. Communication about policy or program through channels with other government organizations happens infrequently, i.e., one to four times a year. Contacts with the industry about policy, however, tend to take place more than once a month. Professional publications, the news media, the trade press and FDA publications (such as Federal Register statements) are used at least weekly for policy and program information.

All "Inside FDA" channels, both one-to-one and meetings, were used more to get information about policy and program matters than to give it. In meetings at the division and agency level, about three-fourths of the exchanges resulted in getting information. Policy and program communication within HHS, but outside FDA, involves getting more than giving. When communicating with federal agencies outside the department, the balance is virtually even. Communication with non-federal governments and private industry results in giving information.

The values assigned to the communication channels for policy and program information were moderately high, and not many respondents took the opportunity to identify a policy and program communication channel that "could and should be improved." Those who did, however, concentrated on channels inside FDA, and the most frequently mentioned channel was the "Federal Register, FDA Talk Papers, etc." This contrasts with the response on science communication when professional meetings and other outside channels were emphasized.

SCIENCE/POLICY INTERFACE

The survey also contained questions about the scientists' perception of the interface between science and policy in FDA. Results show that respondents see their science activities occasionally affected moderately by changes in policy; but they see policy occasionally affected only slightly by their science. Over 50% of the respondents felt no change should be made in the role that policy considerations play in directing science activities, yet nearly 75% think science should play a greater role in policy formulation.

ADDRESSING FDA'S MOST URGENT NEEDS: A TEN POINT PLAN

FDA is establishing a ten-point program to meet the most urgent needs facing the Agency and the public. This plan is designed to identify global priorities and directions necessary for the Agency to prepare itself for the challenges of today and of the 21st Century.

1. New Drug Review Process. FDA will make significant improvements in its new drug review process for human drugs, with the aim of further accelerating the review process while improving quality. FDA will begin by efficiently, effectively, and sensitively taking the following actions: implementing new regulations governing applications to market new drugs and drug experimentation; developing new models for conducting of new drug application reviews; reducing backlogs; enhancing the use of automated data systems, and fully implementing the new program for approving abbreviated applications to market generic drugs.

2. Medical Device Program. FDA will prepare specific recommendations to respond efficiently, effectively, and sensitively to the legitimate criticisms that have been made about the Agency's implementation of the Medical Device Amendments of 1976. Special attention will be directed to those issues relating to bringing new products to market.

3. Post-marketing Surveillance. FDA will strengthen signficantly its post-marketing surveillance activities to enchance consumer protection against new and unforeseen risks with marketed products. Actions will include: working with health professionals to promote prompt, more complete reporting of adverse drug reactions; successfully implementing the new drug and device regulations; and upgrading current programs where necessary, to ensure adequate surveillance of all human drugs, biologics, new animal drugs, and food products.

4. Risk Assessment. FDA will develop a comprehensive program to evaluate and test, where practicable, the assumptions used in risk assessment. The Agency will focus primarily on assessing the risk to humans of compounds contained in the food supply that have been found to cause cancer in laboratory animals. This program will be coordinated with other Federal agencies having an interest in risk assessment.

5. Risk Management. FDA will make significant improvements in its risk management processes, with particular emphasis on early analysis of options, optimal utilization of FDA's full range of regulatory tools (i.e., education, enforcement, regulation, and voluntary compliance), organization of FDA's field operations, and coordination with other Federal, State and local agencies.

6. Food Safety. FDA will continue to work toward the resolution of food safety issues.

7. Nutrition. FDA will significantly broaden its nutrition program to advance the science of nutrition, increase consumer awareness about nutrition, and provide continued assurance of the nutritional quality of the Nation's food supply. FDA will coordinate these activities with the United States Department of Agriculture (USDA) and the National Institutes of Health.

8. New Technologies. FDA will undertake to develop specialized internal capabilities in those new technologies most likely to dominate new medical developments and changes in the food supply, with particular emphasis on biotechnology and microelectronics.

9. Health Fraud. FDA will implement a significantly broadened initiative aimed at reducing health fraud, including both increased emphasis on enforcement activities and increased efforts at achieving consumer and health professional awareness. Particular attention will be given to focused efforts on health fraud creating health hazards and life-threatening dangers.

10. Internal Management. FDA will make significant improvements in its own internal management, particularly in the areas of career advancement, information systems, laboratory research programs, resource allocation and science base. Particular attention will be given to the Commissioner's Advancement Program designed to meet the personnel needs of FDA.

APPENDIX 3

FOOD AND DRUG ADMINISTRATION
U.S. PUBLIC HEALTH SERVICE
DEPARTMENT OF HEALTH AND HUMAN SERVICES

"A PLAN FOR ACTION"

JULY 1985

EXECUTIVE SUMMARY

This Action Plan is designed to fulfill the Secretary's charge of preparing FDA for the challenges of today and of the 21st century. The plan designates FDA's highest priorities and charts a broad course for the Agency's policy and management directions in the years ahead. The plan was based on extensive meetings that the Commissioner held with persons from both inside and outside the Agency. The Action Plan may be summarized as follows:

1. **NEW DRUG REVIEW PROCESS.** FDA will make significant improvements in its new drug review process for human drugs, with the aim of further accelerating the review process while improving quality. FDA will begin by efficiently, effectively, and sensitively taking the following actions: implementing the new IND/NDA regulations; developing new models for conducting NDA reviews; reducing the backlog of supplemental NDAs; enhancing the use of automated data systems; and fully implementing the new program for post-1962 ANDAs.

2. **MEDICAL DEVICE PROGRAM.** FDA will prepare specific recommendations to respond efficiently, effectively, and sensitively to the legitimate criticisms that have been made about the Agency's implementation of the Medical Device Amendments of 1976. Special attention will be directed to those issues relating to bringing new products to market: premarket notifications [510(k)s]; premarket approval (PMA) applications; preamendments PMAs; and investigational device exemptions (IDEs).

3. **POSTMARKETING SURVEILLANCE.** FDA will strengthen significantly its postmarketing surveillance activities to enhance consumer protection against new and unforeseen risks with marketed products. Actions will include: working with health professionals to promote prompt, more complete reporting of adverse drug reactions; successfully implementing the new drug and device regulations; and upgrading current programs, where necessary, to ensure adequate surveillance of all human drugs, biologics, new animal drugs, and food products.

4. **RISK ASSESSMENT.** FDA will develop a comprehensive program to evaluate and test, where practicable, the assumptions used in risk assessment. The Agency will focus primarily on assessing the risk to humans of compounds contained in the food supply that have been found to cause cancer in laboratory animals. This program will be coordinated with other Federal agencies having an interest in risk assessment.

5. **RISK MANAGEMENT.** FDA will make significant improvements in its risk management processes, with particular emphasis on early analysis of options, optimal utilization of FDA's full range of regulatory tools (i.e., education, enforcement, regulation, and voluntary compliance), organization of FDA's field operations, and coordination with other Federal, state and local agencies.

6. **FOOD SAFETY.** FDA will continue to work toward the resolution of food safety issues by administrative or legislative means, as appropriate.

7. **NUTRITION.** FDA will significantly broaden its nutrition program to advance the science of nutrition, increase consumer awareness about nutrition, and provide continued assurance of the nutritional quality of the Nation's food supply. FDA will coordinate these activities with the United States Department of Agriculture (USDA) and the National Institutes of Health (NIH).

8. **NEW TECHNOLOGIES.** FDA will undertake to develop specialized internal capabilities in those new technologies most likely to dominate new medical developments and changes in the food supply, with particular emphasis on biotechnology and microelectronics.

9. **HEALTH FRAUD.** FDA will implement a significantly broadened initiative aimed at reducing health fraud, including both increased emphasis on enforcement activities and increased efforts at achieving consumer and health professional awareness. Particular attention will be given to focused efforts on health fraud creating health hazards and life threatening dangers.

10. **INTERNAL MANAGEMENT.** FDA will make significant improvements in its own internal management, particularly in the areas of career advancement, information systems, laboratory research programs, resource allocation and science base. Particular attention will be given to the Commissioner's Advancement Program designed to meet the personnel needs of the FDA.

The Agency has profited from the analysis that has led to the development of this Action Plan and looks forward to implementing these programs under its Implementation Plan. FDA is confident that these steps will not only prepare the Agency for the 21st century, but will also strengthen the Agency's current programs. The Action Plan is described in greater detail in the body of this report.

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INTRODUCTION

The decision to develop an Action Plan emanated from discussions between the Secretary and the Commissioner. The following charge from the Secretary provided the framework for this planning activity:

> *As Secretary of Health and Human Services, I charge the Commissioner to lead in a planning process that will prepare the Food and Drug Administration for the challenges of the 21st century; to build FDA's science base to the same perceived and actual quality as NIH in those areas necessary to fulfill the Agency's mission; and to use science as the major method for decision-making. In fulfilling this charge, the Commissioner should meet with consumers, academicians, health professionals, and members of the regulated industry, as well as former Commissioners.*
>
> *- Margaret M. Heckler.*

Acceptance by the Food and Drug Administration (FDA or the Agency) of the Secretary's charge confers a public trust as well as a high responsibility. Under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and related laws, the Agency is accountable to the public for ensuring that the Nation's food supply is safe, wholesome and nutritious; that its pharmaceutical, biological, and medical device products are safe and effective; that its cosmetics are safe; that the use of radiological products does not result in unnecessary exposure to radiation; and that all FDA-regulated products are honestly promoted and labeled. The discharge of this public trust and responsibility involves the overseeing and regulation of tens of thousands of firms and hundreds of thousands of products. In total, the FDA regulates products accounting for almost 25 cents of every consumer dollar spent.

The Secretary's charge also recognizes clearly the necessity to chart a steady course through a sea of perplexing problems, competing priorities, and finite resources. Moreover, the future is certain to be marked by rapid technological change and by increased and sometimes conflicting expectations of FDA by the Congress, the business sector, the scientific community, and the public at large.

It is important to recognize at this juncture the Agency's history, its roots, and its image. FDA has traditionally been a law enforcement agency whose scientific base directly supported its law enforcement activity. Acceptance of this mission resulted in the recruitment of large numbers of investigators and analysts in the field offices as compared to headquarters research and scientific support personnel. Investigative activity leading to enforcement actions on a case-by-case basis was the foundation of this approach. Such actions served the public and the Agency exceedingly well during its early years by ensuring the safety of foods, drugs, and cosmetics initially regulated by FDA.

During the Sixties and Seventies, FDA was assigned a number of other laws to administer, and changes occurred in the FD&C Act that influenced FDA and produced significant new demands on the Agency. As society's expectations of FDA changed and these laws were modified, FDA's strategy of establishing policy largely through case-by-case enforcement actions was changed to rely primarily on the more orderly, though more ponderous, process of regulation development through notice and comment rulemaking procedures. Most recently FDA has given education and voluntary compliance a more prominent role in its armamentarium of methods used to ensure the safety and effectiveness of regulated products.

The mission of FDA may be stated succinctly as follows:

> FDA is a public health agency whose primary goals are to protect and promote the public health and well-being of consumers through the effective use and enforcement of all public health and consumer protection authorities available to the Agency.

In fulfilling this mission, the FDA must rely on a firm scientific foundation and must implement its decisions through an appropriately balanced combination of education, enforcement, regulation, and voluntary compliance activities. The particular method(s) used depends on the case at hand. Public health protection is accomplished through careful, premarket review of new products as well as through effective monitoring, detection, and corrective actions against violative products and firms. Public health promotion can be achieved through educating consumers in the prevention of disease, by facilitating the development of new products that will aid in overcoming or combating disease, and by informing both consumers and health professionals about the responsible use of safe and effective health care products. These fundamental principles of public health protection and public health promotion underlie FDA's programs and decision-making processes.

Thus, the Secretary's insightful charge, the Agency's history and capacity to adapt over time to new challenges, and a clear sense of mission have enabled FDA to undertake successfully a comprehensive planning process to renew itself and to commit itself to solving the problems it confronts now and in the future.

PLANNING FOR RENEWAL

To fulfill the Secretary's charge, the Agency embarked in August 1984 on a planning process designed to prepare itself for the challenges of today and of the 21st century. (See Appendix I, "The Action Plan Development Process.") As the Nation's oldest consumer protection Agency, FDA began with the premise that it was already strong and that the Agency needed to renew and build upon that strength rather than tear down and then rebuild itself. The first step was an exploration both of internal management and of external perception to determine how the Agency might meet the opportunities, challenges, and responsibilities of future months, years, and decades and how the FDA could address them most efficiently, effectively, and sensitively. This analysis is particularly relevant in this time of increasingly limited resources.

Two methods of gathering this information were used: internal (Pathway A) and external (Pathway B). To accomplish the internal evaluation, six task forces of FDA personnel were charged to develop recommendations for personnel development, information management, resource allocation, scientific base, facilities, and regulatory approaches. The enthusiastic response by these task forces and the positive, constructive nature of their many recommendations reflects the strength of the Agency and its capacity for self-improvement. The external evaluation was viewed as an essential method to gather perceptions from the community FDA serves. Nineteen meetings were held with 54 groups, including all the constituencies mentioned in the Secretary's charge. These outside groups presented their views candidly and responded thoughtfully to questions posed by FDA, again reflecting a positive attitude toward finding workable solutions to the problems at hand. It was concluded that this planning process provided an opportunity to develop a new beginning, not by the drastic overhaul of a weak agency, but through the renewal of a strong one.

The review of these recommendations has been a profound lesson in humility. The challenges are real and complex. The suggestions and ideas gathered have impressive merit. Many of the challenges can be met within existing resources, but all require the time and attention of an agency already faced with the need to balance many competing priorities. Solutions will not be easy or simple. Furthermore, it was quickly realized that neither the Commissioner nor the Agency could simply set aside existing responsibilities, or stop enforcing some selected part of the law, in order to work on new initiatives. Accordingly, it has been necessary to make tough decisions and prioritize FDA's actions to ensure that the Agency's commitments made in this plan can and will definitely be effected on a timely basis.

PHILOSOPHICAL CONSIDERATIONS

In developing a plan for action, the Agency has followed the regulatory goals and priorities enunciated by the Secretary and the Administration. In this regard, the Agency has based many of its conclusions on the following philosophical considerations:

a. Public health protection and public health promotion must remain FDA's highest priorities. FDA must continue the assurance of safety and effectiveness while fostering technological innovation.

b. FDA must utilize its full range of tools to carry out its responsibilities under the law, including education, enforcement, regulation, voluntary compliance, or responsible combinations of them. Promulgation of each new regulation must be coupled with an effective enforcement strategy.

c. The quality of the product review processes within FDA must be high. Those processes must employ hands-on, state-of-the-art science and be supplemented by effective postmarketing surveillance systems. Decisions must be made carefully and expeditiously.

d. FDA must maintain a strong intramural science base with a particular emphasis on conducting appropriate research in those scientific areas needed for risk assessment. A deeper and more quantitative understanding of animal toxicology and its relevance to humans is vital. Emphasis should also be directed to the most dominant new technologies, especially biotechnology and microelectronics.

e. FDA must recognize that for some matters it can no longer rely solely on its own scientists either for technical expertise across the board or for completing new product reviews in a timely fashion. Given the rapid advances in medical technology, increasing workloads, and finite resources, FDA must work more closely with the larger scientific community both in collaborative science and in the product review processes. This collaboration will provide the additional benefit of increasing FDA's capacity to interact with scientists in academia and industry, as well as with health professionals, on a peer relationship basis.

f. FDA must communicate fully with and be responsible to diverse groups with particular emphasis on the maintenance of a strong scientific base for decision-making in an open environment. Ongoing forums for open communications with consumers, academia, state and local health officials, industry, and health professional groups must be expanded and strengthened in a significant fashion. In this regard, FDA should consciously build interdependent constituencies to foster consensus formation and broad support for important new initiatives.

g. FDA must make significant improvements in its internal management of Agency processes. Substantial effort should be placed on personnel development and management systems, with particular emphasis on information systems, coordination of science (especially in the field of toxicology), and the configuration of FDA's field offices. This approach is designed to augment quality and productivity while increasing job satisfaction of FDA employees.

h. FDA's system for resource allocation within the Agency must be upgraded to accommodate fiscal constraints over the near term. Modifications in the resource allocation system must be fair and equitable. Budgetary cuts should not simply be absorbed Agency-wide on a pro rata basis. Rather, resources need to be reallocated to reflect program priorities, with some programs or activities receiving increased resources and other non-mandatory programs or activities being further reduced or eliminated.

i. FDA must be bold and willing to explore, develop and implement appropriate new methods for fulfilling its mission, especially when new technologies mandate change. For example, new diseases such as Acquired Immune Deficiency Syndrome (AIDS) will continue to emerge, and vigorous action must be undertaken to enable effective diagnostic tests and therapeutic entities and/or vaccines to be approved in a timely fashion.

ADDRESSING FDA'S MOST URGENT NEEDS: A TEN POINT PLAN

Based on these philosophical considerations, and taking into account the many recommendations received from the internal and external groups, FDA is establishing a ten-point program to meet the most urgent needs facing the Agency and the public. This plan is designed to identify global priorities and directions necessary for the Agency to prepare itself for the challenges of today and of the 21st Century.

1. **NEW DRUG REVIEW PROCESS.** FDA will make significant improvements in its new drug review process for human drugs, with the aim of further accelerating the review process while improving quality. FDA will begin by efficiently, effectively, and sensitively taking the following actions: implementing the new IND/NDA regulations; developing new models for conducting NDA reviews; reducing the backlog of supplemental NDAs; enhancing the use of automated data systems; and fully implementing the new program for post-1962 ANDAs.

2. **MEDICAL DEVICE PROGRAM.** FDA will prepare specific recommendations to respond efficiently, effectively, and sensitively to the legitimate criticisms that have been made about the Agency's implementation of the Medical Device Amendments of 1976. Special attention will be directed to those issues relating to bringing new products to market: premarket notifications (510(k)s); premarket approval (PMA) applications; preamendments PMAs; and investigational device exemptions (IDEs).

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reactions; successfully implementing the new drug and device regulations; and upgrading current programs, where necessary, to ensure adequate surveillance of all human drugs, biologics, new animal drugs, and food products.

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10. INTERNAL MANAGEMENT. FDA will make significant improvements in its own internal management, particularly in the areas of career advancement, information systems, laboratory research programs, resource allocation and science base. Particular attention will be given to the Commissioner's Advancement Program designed to meet the personnel needs of the FDA.

As noted above, this plan is designed to chart global priorities and directions for macro-management of the Agency. It is not meant to be all-inclusive of Agency activities. In addition to implementing this plan, the Agency will continue to engage in its full range of programs necessary to meet its responsibilities under the law in regulating foods, drugs, cosmetics, medical devices, biologics, and radiological products. The plan, therefore, does not address many of FDA's ongoing programs, such as the over-the-counter (OTC) drug review, orphan drugs, classification of medical devices, food additive petitions, veterinary drugs and feeds, and international cooperation and communication. FDA will be moving forward in these and other areas concurrent with implementation of the Action Plan.

FDA also recognizes that this plan does not address all of the specific recommendations advanced by the internal task forces and outside groups. The Agency will continue to evaluate the many specific recommendations that were received and will implement on a continuing basis those recommendations that the Agency finds meritorious.

In conclusion, this Action Plan is designed to chart a broad course for the Agency and to guide its policy and management directions now and in the years ahead. Each of the ten high priority program areas is discussed in greater detail below.

IMPLEMENTATION

Through a carefully crafted Implementation Plan containing specific commitments and deadlines, the Agency's line managers will be responsible for ensuring the successful execution of the Action Plan initiatives under their respective areas of authority and responsibility. Each line manager will also be responsible for reporting periodically to the Commissioner on the progress of the various Action Plan items. In conjunction with these efforts, the Office of Planning and Evaluation (OPE) is establishing reporting mechanisms and evaluation requirements to ensure that the implementation and impact of the Action Plan are communicated to the Commissioner and line managers on a timely basis.

1. NEW DRUG REVIEW PROCESS

- *FDA will make significant improvements in its new drug review process for human drugs, with the aim of further accelerating the review process while improving quality. FDA will begin by efficiently, effectively, and sensitively taking the following actions: implementing the new IND/NDA regulations; developing new models for conducting NDA reviews; reducing the backlog of supplemental NDAs; enhancing the use of automated data systems; and fully implementing the new program for post-1962 ANDAs.*

FDA continues to receive substantial criticism that it is too slow in approving new human drugs. While FDA does not believe all of this criticism is merited, the Agency has come to the conclusion, following careful review and thought, that some significant actions can be taken now to shorten the time required to conduct its premarket review of new human drugs, while increasing the quality of the review process. FDA also believes that the law leaves substantial room for innovation and exploration of different ways and means to improve the drug review process. The Agency, therefore, is taking the following actions:

INTRAMURAL MODELS FOR DRUG REVIEWS

FDA's Center for Drugs and Biologics (CDB) will promptly develop and implement pilot programs in at least two drug reviewing divisions designed to facilitate the drug review process while maximizing scientific quality. While a large variety of approaches will be explored, two important approaches involve: (1) improved access to high quality reviewers and (2) elimination of inefficiencies in the review process.

- While FDA is fortunate to have many highly qualified reviewers who devote full time to drug regulation, it is probable that there are many additional scientists who would welcome the opportunity to participate in the drug regulatory process as a part, but not the entirety, of their professional lives.

Access to these scientists would not only increase the quality staffing of the review process, but would also involve a group of scientists actively engaged in research and/or patient care. Three approaches will be undertaken.

a. CDB will seek to increase use of individual outside expert reviewers in the review process who would serve on a consultant basis. Such reviewers have been utilized in the past to some degree, particularly to obtain expertise that is not available in-house, and such use will be expanded.

b. CDB will seek to recruit as full-time employees scientists who can carry out both scientific research and regulatory activities. Scientists with this type of background are already present in the Center to some degree, particularly in the biologics area, and additional recruitment efforts will be employed.

c. CDB will develop an FDA fellowship program. This would become a funding source for academic scientists, principally in nearby institutions, who would be willing to participate actively (at least two days per week) in the regulatory process while also pursuing their academic careers.

- CDB will examine its procedures in a variety of ways, with the view towards improving management efficiency. This will include:

  a. Examining areas in which delegation of sign-off authority can be undertaken to eliminate a level of formal review, without allowing unacceptable divergency of policy and standards.

  b. Identification and elimination of any redundant reviews, reports, or summaries that do not contribute to the quality of the review process.

Successful initiatives will be extended to other divisions as appropriate.

IND/NDA REWRITE IMPLEMENTATION

- CDB will implement in a timely, efficient, and effective manner the drug review process modifications provided for in the recently developed revisions to the NDA regulations and will continue the work to implement fully the IND regulations in the near future. Specifically, in conjunction with implementation of the NDA Rewrite, CDB will ensure: (1) that operating instructions for industry and training instructions for CDB's professional review staff are developed; and (2) that earlier office management participation in the NDA review process is instituted to accomplish the following objectives:

  a. Through the increased use of FDA guidance and standardized formatting of applications, drug sponsors will have a clearer understanding of Agency requirements. This in turn will reduce the application's time at FDA because the application will come to the Agency in a form suitable for complete and expeditious review.

  b. Through the increased use of data tabulations and summaries, FDA reviewers can focus their attention on more concise presentations of relevant information, thus saving review time.

  c. By also reducing the number of case report forms to those critical to the safety and effectiveness review, Agency reviewers will be able to focus their attention immediately on the most significant reports, thus further saving time in their review.

  d. By accepting relevant clinical data generated outside the United States that meet acceptable criteria, this may obviate the need, in certain instances, for redundant and more costly studies having to be performed in the U.S. in order for a drug sponsor to obtain marketing approval.

AUTOMATED DATA SYSTEMS

- CDB will also explore and implement the appropriate use of automated data systems in an effort to enhance the quality of the drug review process and to reduce the non-essential data handling burdens both of the regulated industry and of FDA.

EFFECTIVENESS SUPPLEMENTS

- In addition to improving the review process for original NDAs, it is also important for FDA to improve its process review of effectiveness supplements to original applications. These supplements cover such important effectiveness enhancing areas as new indications for use, new dosing regimens and new routes of administration for drugs of proven safety. Accordingly, CDB will develop and implement as soon as possible a substantially upgraded process for reviewing and modifying effectiveness supplements. The program should include:
  - a. the development of a system for monitoring the processing and reviewing of these supplements;
  - b. an assessment of recent performance in supplement review and the development of specific goals for improvement;
  - c. the establishment of a system of priorities for supplement review; and
  - d. the determination of which supplements can be delegated to Division Directors for final action and which require Office level review.

USE OF EXTERNAL ORGANIZATIONS

In addition to taking these steps to improve the current process for reviewing and acting on new drug applications, the Agency also believes that involvement of an outside party might further contribute to the process. Therefore, CDB will explore with the Institute of Medicine (IOM) areas in which the IOM, or other appropriate outside groups, might be able to support the Agency's efforts; possible roles include analysis of specific scientific problems by forming expert review groups or analyses of more global issues.

ANDA IMPLEMENTATION

Finally, CDB will continue to devote a high level of attention to its review of generic drugs under the abbreviated new drug application (ANDA) procedures. Title I of the Drug Price Competition and Patent Restoration Act of 1984 greatly expanded the number of generic drugs that are eligible for marketing approval. The Agency has already established a system for handling the increase in workload. Since the anticipated surge in the number of ANDAs submitted has become a reality, CDB management will closely monitor the progress of the ANDA review process and will ensure that necessary resources are devoted to it. CDB will also prepare new ANDA regulations necessary to implement Title I of the new law.

To complement this Title I effort, FDA's Office of Health Affairs (OHA), in cooperation with the Office of Patents and Trademarks of the Department of Commerce, will be responsible for the effective implementation of Title II of the new law regarding patent term restoration for human drugs, devices and food additives. In this way, FDA will help to ensure that the law's dual objectives of fostering competition and preserving incentives for innovation are achieved.

2. MEDICAL DEVICE PROGRAM

- *FDA will prepare specific recommendations to respond efficiently, effectively, and sensitively to the legitimate criticisms that have been made about the Agency's implementation of the Medical Device Amendments of 1976. Special attention will be directed to those issues relating to bringing new products to market: premarket notifica-tions [510(k)s]; premarket approval (PMA) applications; preamendments PMAs; and investigational device exemp-tions.*

The Medical Device Amendments of 1976 brought expanded new authorities and responsibilities for the regulation of medical devices by FDA. Eight years of experience with this legislation have resulted in significant achievements in implementing a major, complex piece of consumer health legislation. This legislation embodied many novel approaches to regulation. Such approaches included classification of devices into Class I, II or III, premarket notification [510(k)s], product development protocols, and banned devices. Implementing regulations have continued in that same spirit, providing flexible regulatory requirements to Investigational Device Exemptions (IDEs) and Good Manufacturing Practices regulations (GMPs).

Despite this progress, experience with the 1976 Medical Device Amendments leaves many unanswered questions about how best to regulate medical devices without inhibiting new product development. The Medical Device Amendments provided for a very comprehensive regulatory scheme, certain provisions of which have been difficult to implement, as originally conceived, within available resources. As a result, a gap has developed between Congressional expectations for this program and the reality of its implementation in light of public health priorities.

Now is the time to reassess fully the Medical Device Amendments and FDA policies associated with them. FDA must consider changes to its regulations and policies, as well as recommend possible changes to the law, that will better prepare the Agency to continue both its consumer protection and its technology transfer responsibilities.

The management of the FDA's Center for Devices and Radiological Health (CDRH) has recognized these difficulties and has already begun to consider necessary changes through the establishment of several Agency-wide task forces. This self-generated effort will be incorporated directly as an important element of this Action Plan.

Accordingly, based on these task force efforts, CDRH will complete a comprehensive review of the medical device program and will prepare a report of findings and recommendations. The report will address the current status of implementation of the device amendments and will make specific recommendations designed to enhance FDA's abilities to carry out its public health responsibilities with maximum efficiency, effectiveness, and sensitivity. These recommendations will include options for regulatory changes; proposed policy and procedural changes; and legislative proposals, if necessary. The proposed plans for change will include built-in evaluation programs to assure on-going assessment of the impact of change.

This comprehensive review of the device program will address the following significant objectives and goals.

PREMARKET NOTIFICATION [510(k)] PROCESS

The premarket notification [510(k)] process allows a company to market a device, without submitting a premarket approval (PMA) application, if the device is substantially equivalent to a device that was marketed prior to enactment of the 1976 Amendments. The law provides FDA with 90 days to review a premarket notification submission.

- **CLASS I EXEMPTION CRITERIA.** The law further provides that submission of a premarket notification is unnecessary for those Class I devices that FDA exempts from 510(k) filing. FDA will develop exemption criteria for the submission of Class I 510(k)s and apply those criteria to classification regulations that have yet to be finalized. These exemption criteria will result appropriately in fewer 510(k)s being submitted, thus freeing up some CDRH resources for the review of more complex 510(k)s.
- **CHANGES TO MARKETED PRODUCTS.** CDRH will develop criteria delineating manufacturers' responsibilities for validating changes to a marketed device and FDA's responsibilities in reviewing those changes in the 510(k) process. This will result in clearer policy and guidance for industry and FDA reviewers.
- **POLICY ON SUBSTANTIAL EQUIVALENCE.** CDRH will develop a policy document for use by internal reviewers to determine when a device is substantially equivalent to another device. This will result in greater consistency among the divisions in the Office of Device Evaluation and will clarify CDRH policy for determining substantial equivalence.

PREMARKET APPROVAL (PMA) PROCESS

The premarket approval (PMA) process for medical devices is analogous to the new drug review process. By law, the PMA process applies to Class III devices marketed after the 1976 Amendments and, as described further below, applies on a retrospective basis to preamendments Class III devices when called for by FDA.

- **PROCEDURAL REGULATIONS.** FDA will finalize and implement procedural regulations governing the PMA process. The regulations are intended both to promote greater consistency in the processing of PMAs and to provide sponsors with greater clarity of the procedures by which PMAs are reviewed.
- **PMA WORKLOAD.** CDRH will review its PMA workload, including consideration of a legislative change to classify "transitional" products (i.e., those products regulated as new drugs prior to the 1976 Amendments) in the appropriate classification category based on their potential risks. Because the review of transitional products uses approximately 25% of the Center's product review resources, this could result in significant savings, thus freeing resources for the more efficient review of new technologies. FDA will also evaluate its procedures to attain as many of these objectives as possible administratively.
- **PANEL REVIEW OF SUPPLEMENTS.** CDRH will issue guidance to internal reviewers regarding when supplements need to be taken to advisory panels. This should help eliminate unnecessary advisory panel reviews and thereby reduce review time. As described earlier in this Action Plan, the Agency is also placing increased emphasis on supplemental new drug applications, thereby focusing on supplements in general.

PREAMENDMENT PMAs

As noted, the law requires FDA to undertake a retrospective "premarket review" on a product category basis of Class III devices marketed before the 1976 Amendments.

- **WORKLOAD MANAGEMENT.** CDRH will pursue a flexible approach regarding its retrospective review of Class III devices that were marketed prior to enactment of the 1976 Amendments. This flexible approach will include refining and weighting the factors FDA uses to identify high priority products, specifying those that pose the greatest potential hazards to public health, and pursuing legislative change, as appropriate, that permits rather than requires FDA to call for PMAs for preamendments Class III devices.

INVESTIGATIONAL DEVICE RESEARCH

FDA regulations separate investigational device research into "significant risk" and "non-significant risk" categories. Although both require investigational device exemptions (IDEs), only research on significant risk devices is monitored by FDA; research on non-significant risk devices is delegated to institutional review boards (IRBs). This allows CDRH to focus its research monitoring efforts on those types of research where such oversight is most warranted.

- **RESEARCH CATEGORIES**. CDRH will re-evaluate categories of studies subject to IDE requirements (such as feasibility studies, sponsor/investigator studies, and studies of new uses for approved devices) and will consider whether abbreviated requirements should be applied to any of these research categories. These abbreviated procedures would parallel those currently applicable to studies on non-significant risk devices.
- **EDUCATIONAL EFFORTS.** CDRH will initiate educational efforts to ensure that "non-significant risk" studies are being monitored adequately by IRBs and to ensure that sponsors and the involved clinical community are aware of their responsibilities for all types of investigational device studies. This will be accomplished by issuing educational packages to IRBs and sponsors of nonsignificant risk studies. CDRH will also issue general guidance to the clinical community on conducting clinical trials of medical devices and to sponsors on conducting

clinical trials of specific types of devices. In conducting an educational program for IRBs, CDRH will coordinate with OHA and NIH.

3. POSTMARKETING SURVEILLANCE

- *FDA will strengthen significantly its postmarketing surveillance activities to enhance consumer protection against new and unforeseen risks with marketed products. Actions will include: working with health professionals to promote prompt, more complete reporting of adverse drug reactions; successfully implementing the new drug and device regulations; and upgrading current programs, where necessary, to ensure adequate surveillance of all human drugs, biologics, new animal drugs, and food products.*

FDA's responsibilities do not end when a new product is marketed. The Agency is charged with assuring that the product will be safe in actual use. Postmarketing surveillance is the monitoring and assessment of product performance after approval and is an important part of FDA's mission. For purposes of this Action Plan, the Agency has selected human drugs and devices as those areas most critical in postmarketing surveillance activities, with emphasis also placed on biologics, new animal drugs, and food products.

HUMAN DRUGS

Human drugs undergo extensive and costly testing and review prior to approval. Human studies are based on well controlled clinical trials to demonstrate safety and efficacy. Thus, when a drug is marketed there is considerable evidence that it will be useful while not causing unacceptable harm.

However, it must be recognized that premarket testing cannot provide complete assurance or information. This is because of practical limitations in the conduct of human trials. Clinical trials generally involve fewer than 2000 patients and seldom last more than 3 years. Thus, they lack the ability to detect uncommon severe side effects and delayed effects of chronic administration. Additionally, patients enrolled in clinical trials usually have uncomplicated diseases and are drawn from a narrow age group. For this reason, premarket testing data often do not address special patient populations, such as pregnant women, children, the elderly and those with complicated conditions requiring multiple drugs. Yet, these groups may well be exposed to a new drug once it is marketed.

Thus, the crucial role of postmarketing surveillance is to provide additional safety information that cannot realistically be developed prior to drug approval. One key to conducting useful surveillance is the maintenance of a system for adverse drug reaction (ADR) reporting. Analyses of the ADR system have shown that it can generate postmarketing signals effectively if it receives the proper reports from the health professional community and strong management from FDA.

The history of ADR reporting at FDA began in the late 1950's and early 1960's when the Agency took over an aplastic anemia and chloramphenicol registry from the American Medical Association. The 1962 revisions of the FD&C Act required industry to report ADRs to the FDA. Since the ADR system was computerized in 1969, over 220,000 reports have accumulated. In recent years the annual number of reports received has climbed from 10,000 to more than 40,000.

The importance of an FDA system for ADR reporting has been emphasized in numerous reviews of the system, both external and internal. Most recently, in 1983, an ADR Task Force in the Center for Drugs and Biologics (CDB) analyzed the ADR reporting program. It found major procedural problems in the way reports were processed and used; the system was backlogged and computer equipment was outdated and in some ways inadequate. Retrieval of some information was also cumbersome.

As a result of the Task Force report and other critiques of the system, substantial improvements in the ADR system were made in 1984. Thus, reports are now entered into the system more rapidly, and backlogs have become minimal; new data processing equipment allows for more efficient data entry and retrieval. In addition, streamlined procedures for identifying warning signals and generating detailed aggregate analyses are being put in place and these procedures are expected to be modified further based on experience gained. Electronic transfer of data from industry is also being tested. These changes are expected to augment the system's capacity to receive and use reports. Changes in the new drug application regulation revisions (NDA Rewrite) will further facilitate triaging and reviewing reports from industry. Finally, a reorganized and expanded staff is helping to ensure that the data received by the system can and will be used as efficiently as possible. Nevertheless, further improvements are needed.

A significant shortcoming of the ADR system is underreporting by health professionals. Ultimately, any ADR surveillance system is dependent on the nature and volume of reports submitted to it. Approximately 90% of ADR reports to FDA are from industry, and only about 10% are submitted directly by physicians. Because direct reports from physicians contain a higher proportion of serious reactions than do those received from industry, increased ADR reporting from U.S. physicians should significantly enhance the usefulness of the ADR system.

There are several reasons why physicians do not report more ADRs directly to FDA. The foremost of these is that physicians are not always aware that reporting is important. Limited surveys suggest that fewer than 10% of physicians are aware of the ADR system and that less than half of these have reporting forms readily available. FDA should do more to promote effective reporting. Additionally, feedback of data to the medical community has been limited, in part, because in the past, generation of reports from the system was so difficult. Report forms have also not been readily accessible; although the forms are mailed out three times a year in the *FDA Drug Bulletin*, it is unlikely that physicians frequently retained them.

Experience with infectious disease reporting, much of which is voluntary, suggests that effective promotion depends on continual reinforcement, readily available and simple report forms, and information feedback. All this is best accomplished at the local level. Promotion of ADR reporting by FDA has been national in scope, but more in-depth educational efforts are needed.

- **REPORTING FROM HEALTH PROFESSIONALS.** To address this problem CDB, working through appropriate channels, will contract with State agencies to conduct 2-3 pilot studies of physician-based ADR reporting. These will entail concerted efforts to promote reporting using innovative means in defined areas. The goal is to improve both the quality and quantity of ADR reporting from health professionals. These pilot studies will be designed to:
    a. develop educational and promotional interventions aimed at appropriately increasing physician reporting;
    b. implement interventions through hospitals and the medical community at large;
    c. collect ADR reports and submit these to the FDA; and
    d. evaluate the impact of the interventions.
- **NEW TECHNOLOGIES.** New technologies to facilitate the electronic transfer, entry, and retrieval of ADR data are available. One example of this is the American Medical Association's Medical Information Network (MINET) System. Addition of such technologies to the ADR system would make the system

easier for health professionals to use, and would further speed internal processing, improve accuracy, and reduce the personnel costs of the system. This would, in turn, facilitate the use and improve the value of ADR reports as a tool for postmarketing assessment of drug safety. Accordingly, CDB will experiment with new technologies in its system for processing and retrieving ADR data. In this regard, CDB will consider ways to streamline the ADR reporting form (Form FDA-1639) so as to encourage reporting, speed processing and improve the transmission, entry, and retrieval of submitted materials. Finally, as noted above, feedback to participating health professionals will also be instituted to encourage their active participation.

- **IMPLEMENT NEW REGULATIONS.** The newly revised NDA reporting regulations for approved new drugs improve the ADR reporting system by focusing prompt reporting by industry on those ADRs most likely to signal important safety problems. These include prompt reports of all ADRs that are both "serious" and "unexpected," as defined by the regulations, and of any significant increase in frequency of serious, expected ADRs. CDB will closely monitor implementation of the new system to ensure that reporting patterns are consistent with those regulations. As part of this monitoring effort, CDB will evaluate the first year's activities under the new regulations.

MEDICAL DEVICES

Until very recently, the reporting of adverse effects associated with medical devices was voluntary (except for those products marketed through the premarket approval process). These reports were fed into the Agency's Device Experience Network (DEN). In December 1984, the new Mandatory Device Reporting (MDR) regulation became effective. This regulation requires device manufacturers and importers to report promptly all deaths and serious injuries reasonably associated with medical devices, as well as certain serious device malfunctions.

- **MONITOR MDR REGULATION.** To ensure maximum utility of this system from the start, FDA's Center for Devices and Radiological Health (CDRH) will evaluate the first year of experience with the program, focusing on the number and type of reports received, the usefulness of these reports for other medical device activities, and the impact and effectiveness of the educational efforts designed for manufacturers to help them comply with the new MDR requirements. At the conclusion of that evaluation, CDRH will consult with CDB to determine if improvements made in the drug system are appropriately transferable to the device system, or vice versa.

OTHER SURVEILLANCE PROGRAMS

FDA will strengthen its postmarketing surveillance capabilities in several important areas, as follows:

- **HUMAN DRUGS WITHOUT APPROVED NDA's.** FDA will introduce reporting requirements for significant ADRs associated with human drugs without approved NDAs. (See 50 FR 11478; March 21, 1985.) This will provide consumers with the same level of protection against serious, unexpected ADRs for all human drugs, regardless of NDA status.
- **BIOLOGICS.** FDA will also examine ADR reporting for biologics to determine the need for consistency and uniformity within CDB.
- **NEW ANIMAL DRUGS.** FDA will review its reporting requirements governing new animal drugs, taking into account unique circumstances associated with obtaining these types of reports (e.g., a large segment of reports coming directly from livestock owners rather than from health care professionals).

- **FOODS.** FDA will implement a program to analyze adverse reaction reports associated with foods, food additives, and food ingredients.

With the completion of this review and necessary followup action, FDA will have in place complete, updated programs governing the postmarketing surveillance of human drugs, devices, biologics, new animal drugs, and foods. Thus, consumer protection will be significantly strengthened across these many product areas.

4. RISK ASSESSMENT

- *FDA will develop a comprehensive program to evaluate and test, where practicable, the assumptions used in risk assessment. The Agency will focus primarily on assessing the risk to humans of compounds contained in the food supply that have been found to cause cancer in laboratory animals. This program will be coordinated with other Federal agencies having an interest in risk assessment.*

The ability to make assessments of the long-term consequences of exposure of people to substances, for use either to estimate risk or to perform a risk-benefit analysis, is critical to many important regulatory actions. In addition to its ability to create sound regulatory decisions, any methodology employed must also have the strong confidence of a substantial majority of the scientific community. In focusing on the risk of cancer from substances contained in the food supply, estimates of risk are usually derived using a methodology called quantitative risk assessment. This methodology employs data from epidemiology, animal tests, and other sources (such as *in vitro* or bacterial tests). Because human epidemiological or human experimental data usually are not available in the foods area, animal tests, in which laboratory animals are dosed with high doses (relative to human exposure) of compounds, are the cornerstone of most FDA risk assessments concerning food compounds.

Quantitative risk assessment is generally comprised of four parts, as outlined in recent reports such as the National Academy of Sciences report on "Risk Assessment: Managing the Process" and the Office of Science and Technology Policy's "Chemical Carcinogens: A Review of the Science and its Associated Principles." Each of these four parts of quantitative risk assessment contains significant gaps in information which require the use of assumptions to allow the process to continue.

Examples of some of the important areas in which gaps caused by lack of information must be bridged using assumptions are: (1) quantifying the level of human exposures to agents; (2) evaluating species and tissue differences in the modulation of the effects of chemical agents; (3) estimating the effects of variables such as diet and age; and (4) extrapolating the results of animal data to likely effects on humans. When carefully evaluated, the uncertainty resulting from the use of assumptions such as these can cause the final result to be uncertain by several orders of magnitude.

Given these sources of uncertainty in assessing risk, it has been believed that the most responsible course available to protect the public health adequately is to use very conservative assumptions. This has been the traditional approach generally used by FDA and other Federal regulatory agencies. This process, however, generates higher estimates of risk than would less conservative assumptions. The traditional approach, therefore, leads to Government placing stringent controls over production of and exposure to substances, up to and including a total ban.

In a number of controversial instances, the public debate has actually been over the assumptions used in the risk assessment for a particular substance (although this fact has not always been appreciated). The focus of these debates has been whether the Agency's assessments are based on the best available science. The resulting uncertainty has eroded public confidence in the ability of the FDA to regulate fairly and reasonably.

Rather than dealing with these matters in an unorganized, piecemeal manner, there is a need to develop and implement an organized comprehensive approach to the evaluation of the validity of the assumptions used in risk assessment. Particular attention needs to be directed to the risk of cancer from compounds contained in the food supply; other toxicities need to be addressed also, but as a lower priority. Because of the general use of risk assessment and the commonality of the problems associated with the uncertainty resulting from the assumptions used to fill existing gaps in knowledge, any such approach will be of major interest to many regulatory agencies and will open doors to collaboration and coordination on a broad basis. The Secretary has also emphasized the importance of understanding the assumptions used in risk assessment (see January 25, 1985 memorandum entitled, "Risk Management of Toxic Substances"). FDA's program will be tailored to the regulatory needs of the Agency, with its special authorities and responsibilities.

To achieve this, FDA will take the following actions:

- **COMPREHENSIVE POLICY COMMITTEE.** A Committee will be formed under the leadership of the Director of FDA's National Center for Toxicological Research (NCTR), in conjunction with the Center for Food Safety and Applied Nutrition (CFSAN) and other interested Agency components, to develop a comprehensive plan for evaluation and testing of the assumptions underlying risk assessment, with the goal of reducing the uncertainties attendant to risk assessment, as described above. In developing this plan, the Committee will coordinate with other interested components within the Department, especially other PHS Agencies and the Committee to Coordinate Environmental and Related Programs (CCERP). This plan should include, but not be limited to, a number of subprograms such as:
    a. prioritizing assumptions as to importance and feasibility of resolution by experimentation;
    b. defining measures relevant to human exposure;

c. evaluating the effects of modulatory factors, such as caloric restriction and different stages of development, on the induction of carcinogenesis; and

d. developing models for extrapolating animal test data to humans.

- **IMPLEMENTATION.** To ensure the successful development of this plan, the following procedures will be followed:

  a. NCTR will use as much external peer review as feasible in the evaluation of the program and specific proposals, in an effort to maximize the scientific quality of the proposals and to increase public confidence in the Agency's use of science.

  b. To decrease start-up time and to maximize resources for this purpose, NCTR will begin the redirection of resources into the new program areas cited above as soon as is feasible and implement any organizational changes necessary to reflect the redirection of NCTR resources.

  c. Through a pilot program at NCTR, FDA will develop an agreement for the use, on a contract basis, and in an efficient manner, of university expertise from a variety of disciplines to provide the skills necessary to complement currently available expertise in the development and implementation of the new program. This program will be extended to other Centers as rapidly as feasible.

  d. The Committee will take the lead in coordinating this program with other Agency risk assessment efforts to minimize duplication of effort and to maximize efficient use of scarce Agency research resources. The Committee will identify areas where the resources of other Centers should be utilized.

5. RISK MANAGEMENT

- *FDA will make significant improvements in its risk management processes with particular emphasis on early analysis of options, optimal utilization of FDA's full range of regulatory tools (i.e., education, enforcement, regulation, and voluntary compliance), organization of FDA's field operations, and coordination with other Federal, state, and local agencies.*

The Secretary has identified risk management as a high priority area and has taken steps to implement a coordinated, Department-wide approach (see January 25, 1985 memorandum entitled, "Risk Management of Toxic Substances"). There is no question that FDA, too, needs to maximize the effectiveness of its risk management system so that the Agency can respond promptly and appropriately to new health risks as they emerge. Indeed, the exercise of effective risk management goes to the very heart of FDA's mission. As the Nation's oldest consumer protection agency, foremost among FDA's responsibilities is the duty to protect the public against new and unforeseen risks. Very often the need is urgent and the health concerns critical, even when the available scientific data are not conclusive. In these circumstances, it is FDA's obligation to take whatever action, if any, is appropriate to respond to that risk. Close coordination is critical in this process, between FDA headquarters and field offices, between FDA and other components of the Department, and between FDA and other Federal, State and local agencies.

Effective risk management requires a series of steps. Once a scientific risk assessment has been completed, the Agency must undertake a careful analysis of alternative courses of action and determine the type of Agency response that is most suitable for correcting the risk presented. The scientific risk assessment analysis must be incorporated directly into this decision-making process. In selecting options, FDA must seek optimal utilization of its full range of regulatory tools, including education, enforcement, regulation, voluntary compliance, or some appropriate combination of them. In reviewing these options, FDA needs to consider the views presented by consumers, health professionals, members of the regulated industry, cooperating State and local agencies, and other affected Federal agencies. FDA must also follow through and complete whatever alternative(s) is chosen, in full cooperation with interested components in the Department and other Governmental units. Implementation should also include the ability to make adjustments as circumstances may dictate.

Although FDA has a strong background and tradition in dealing skillfully with risk management issues, the area is so critical that FDA plans to undertake the following additional actions:

- **ASSESSMENT OF MANAGEMENT PROCEDURES.** FDA will assess its current risk management procedures and identify areas for improvement. Particular emphasis will be given to the development of methods for determining which of FDA's available tools (education, enforcement, regulation, voluntary compliance, or some appropriate combination) are optimal for achieving effective management of the particular risk presented. In developing options and strategies on risk management issues, particular attention will be devoted to providing:
    a. a discussion of the assumptions that were necessary beyond the quantitative assessment of the risk;
    b. a discussion of possible, alternative substances available or, if possible, methods by which a substance may be rendered safe or controlled in such a way as to avoid harmful exposure; and

c. a discussion of alternative, non-Federal sources of risk management, including State and local governments or representatives of the private sector.

- **DEVELOPMENT OF PRIORITIES.** FDA will develop priorities in a work plan designing and implementing new procedures for risk management, including providing an opportunity for public discussion and notification as appropriate. The focus of this work plan will be on proposed rulemaking and pre-rulemaking activities. FDA will integrate into this effort its new system developed under Executive Order 12498 for establishing priorities, identifying options, and undertaking long-range regulatory planning.
- **ENFORCEMENT STRATEGIES.** When promulgation of a new regulation is the chosen course of action, FDA will develop a method to couple an effective enforcement strategy with it. Although, as a general principle, new regulations will not be promulgated unless less intrusive means are considered to be inadequate, when such regulations are called for, it is important to ensure that the new regulations are enforced effectively, sensitively, and consistently in order to achieve the desired public health objective.
- **FIELD RESOURCES.** FDA will review its field resources and modify the configuration of the field as necessary to ensure maximum efficiency for risk management purposes.

FDA's Office of Regulatory Affairs (ORA) will take the lead on these risk management initiatives and will work in conjunction with other appropriate FDA units. ORA will also take into account the principles contained in the Secretary's January 25, 1985 memorandum and coordinate its efforts, as necessary, with other interested components of the Department.

6. FOOD SAFETY

- *FDA will continue to work toward the resolution of food safety issues by administrative or legislative means, as appropriate.*

It is essential that the Nation's food safety laws, and the FDA's implementation of them, adequately protect the public. FDA worked closely with the Working Group on Food Safety of the Cabinet Council on Human Resources (1981-83) in an attempt at modernization of related food safety legislation. The Agency continues to support the basic approach outlined by the Working Group.

FDA is interested in the resolution of the following specific food safety issues by administrative or legislative means, as appropriate.

- **CONCEPT OF SAFE.** Current law does not make clear what "safe" means for food, and there is public confusion and ambiguity about how the concept of safety applies in any given case. FDA has attempted to deal with food safety issues as they have arisen, but policies in this area are still not as well developed as may be necessary. Accordingly, the Agency will continue to explore legislative or administrative approaches to refine further and to clarify policies on food safety.
- **PHASE-OUT AUTHORITY.** There is no specific provision in current law for the gradual phase-out of a marketed substance that is being banned for possible long-term adverse effects. Phase-out authority might be considered under appropriate circumstances, such as where: (a) there is no immediate risk to public health; (b) the substance has no reasonably practicable substitute; and (c) an abrupt ban could cause severe disruption to the food supply.
- **RISK-BENEFIT ASSESSMENT.** In general, current law with respect to food additives provides only for the consideration of health risks, not health

benefits. Consideration should be given that health benefits be taken into account in some circumstances.

Even under current law it is possible to address a range of food safety issues utilizing risk assessment procedures. For example, the Agency has employed, and will continue to employ, such procedures in the consideration of:

a. residues in edible tissues of food producing animals that consumed carcinogenic substances (animal drug safety policy); and

b. low levels of carcinogenic constituents of food additives where the additive as a whole is not carcinogenic (constituents policy).

In conclusion, while FDA continues its support for legislative change in the food safety area, the Agency believes that alternative means for achieving many of the objectives of the legislative initiatives can be accomplished with administrative action. These should be explored by appropriate Agency staff and the Office of the General Counsel.

7. NUTRITION

- *FDA will significantly broaden its nutrition program to advance the science of nutrition, increase consumer awareness about nutrition, and provide continued assurance of the nutritional quality of the Nation's food supply. FDA will coordinate these activities with the United States Department of Agriculture (USDA) and the National Institutes of Health (NIH).*

Appropriate nutrition is necessary for optimal growth and development, physical activity, reproduction, recovery from illness, and maintenance of health throughout life. Public interest in nutrition has changed considerably in the past decade. In the first 30 or 40 years of this century, the main nutritional interest of many Americans was in getting enough food to eat and in avoiding such vitamin-deficiency diseases as pellagra, rickets, scurvy and beriberi. Now, although the role of nutrition in health problems is not fully understood, epidemiologic and laboratory studies have begun to offer important insights that may help people make food choices which enhance their prospects of attaining and maintaining health. For example, people have begun to consume less total fat, saturated fat, and cholesterol, and have curtailed their intake of salt to reduce the risk of high blood pressure. A number of recent surveys indicate that people are more interested in nutrition, are more aware of the actions they can take to maintain health through their daily eating patterns, and are changing their nutritional practices. These changes were accompanied by a general increase in awareness of the American public about the prevention of disease through their responsibility for maintenance of good health. Yet, there is much to be done to improve the health status of Americans through nutrition and to reduce nutritional risk factors in the American diet.

Nutrition is an area of major importance to FDA. The Agency's work in this area encompasses the entire spectrum of nutrition-related activities. The issues faced by the Agency are at the cutting edge of national nutrition concerns (e.g., infant formula, weight control products, food fortification, and specially formulated foods for the dietary management of some disease conditions). FDA's research efforts are necessarily more applied than basic in nature and are closely related to the Agency's regulatory program. As an understanding of the relationships between nutritional factors and good health becomes more clearly defined, public interest in nutrition will continue to escalate. Consequently, nutrition will continue to be of high interest to Congress, the food industry, professional associations, and consumers.

NUTRITION INITIATIVES

FDA's Center for Food Safety and Applied Nutrition (CFSAN) will undertake the following initiatives to increase its focus on nutrition. In carrying out these initiatives, CFSAN will coordinate with the United States Department of Agriculture (USDA) and the National Institutes of Health (NIH), as appropriate.

- **SCIENCE OF NUTRITION**. CFSAN should take steps to advance the science of nutrition and to provide continued assurance of the nutritional quality and safety of the Nation's food supply. FDA has a principal Federal responsibility for food safety. As food processing methods and dietary patterns change, the Agency must constantly evaluate and redirect its own programs to provide continued assurance that there is no deterioration in the nutritional adequacy or safety of the food supply.
- **TECHNOLOGIC ADVANCES**. Newly formulated foods or unique processing techniques may have profound effects on the nutritional quality of foods. For

example, labile nutrients may be destroyed as the result of processing, or complexes may be formed which render essential nutrients non-absorbable. CFSAN will develop a strategic plan for strengthening its food science program and to study issues such as the nutritional quality of formulated foods and the effects of food processing on the nutritional integrity and safety of foods. Additionally, factors which may affect nutrient bioavailability either positively or negatively, such as processing or particular combinations of ingredients in food, must be evaluated. This work should include a study of nutrients of public health concern, such as the current collaborative studies on iron bioavailability. FDA must continue to develop new and improved methods for the analysis of nutrients and metabolites in foods for the support of research and regulatory activities. Accordingly, CFSAN will continue to pursue research intended to increase the knowledge base in areas of public health concern that are directly related to the Agency's programs (for example, research on the relationship of dietary fiber consumption to health status) and to use the information developed for regulatory action, when appropriate.

- **ANALYTICAL ISSUES.** CFSAN should continue implementing its plans to establish an integrated nutrition-toxicology program. Objectives should include: the evaluation of optimal nutritional needs of laboratory animals; the determination, in collaboration with other Centers interested in toxicology, of the impact of diet and nutritional status on toxicological end points; and the development of sensitive indications of nutrient toxicity. Some principles can be gleaned from an analysis of human clinical trials, but in many instances, animal studies are essential for evaluation of data related to man.

- **MICROBIOLOGY.** CFSAN will develop a comprehensive approach to the analysis of microbial contamination of food using state-of-the-art conventional and biotechnological methods, with particular emphasis on the newly emerging pathogens and microbial problems accompanying technical modifications of food processing.
- **MONITORING.** CFSAN will support a comprehensive national nutrition monitoring system and conduct surveillance activities that provide information about the nutrient composition of foods eaten, food labeling, medical foods, and public knowledge, attitudes and preferences concerning foods.
- **INTERAGENCY EDUCATIONAL EFFORTS.** As the coordinator of the Surgeon General's Nutrition Objectives for 1990 and a major contributor to the Surgeon General's Report on Nutrition and Health, FDA should continue to play a leadership role in interagency educational programs and work cooperatively with other agencies to help assure that the Federal government speaks with a single clear voice on nutrition activities.
- **HEALTH MESSAGES ON FOOD LABELING.** The Agency believes that there is a public health benefit to providing accurate general information on food labeling concerning the relationship between diet and good health. Accordingly, the Agency is considering mechanisms for appropriate "health messages" on food labeling. These health messages developed by NIH, NCI, FDA, and USDA would contain information concerning how diet can help promote good health and would be for use on foods. This goal will be accomplished under the leadership of the Office of Regulatory Affairs (ORA) and CFSAN, in conjunction with other appropriate Agency components and

the Office of the General Counsel. FDA will also coordinate with NIH and other involved components of the Department.

8. NEW TECHNOLOGIES

- *FDA will undertake to develop specialized internal capabilities in those new technologies most likely to dominate new medical developments and changes in the food supply, with particular emphasis on biotechnology and microelectronics.*

One of the greatest challenges facing FDA in preparing for today and for the 21st century (less than 15 years from today) is keeping pace with the ongoing revolution in medical and food technology. Although FDA cannot expect to maintain internal expertise in all the many new technologies being developed, it is incumbent upon the Agency to build internal capabilities in those areas most likely to dominate new scientific and medical developments. After careful evaluation of this vast field, FDA has determined that special internal emphasis should be placed on biotechnology and microelectronics.

- **BIOTECHNOLOGY.** The discovery of recombinant DNA technology has led to a revolution in biotechnology. Many of the biotechnology products for humans and animals will require approval by FDA, as noted in the recent *Federal Register* notice describing the proposal of the Working Group on Biotechnology of the Domestic Policy Council (49 FR 50856; December 31, 1984). New challenges will face FDA, many of them both uncommon and unexpected today. Particular attention will be directed to new human and animal drugs, vaccines, diagnostic reagents, gene therapy, and modified plants for human consumption. Risk assessment, including model microcosm research and stability of gene products and probes, will require extensive coordination of ongoing research and selective expansion of research efforts. Additionally, FDA must focus on the potential adulteration of food as new plants are developed through biotechnology. Thus, product approval alone is insufficient; a system of postmarketing surveillance must also be developed. Finally, it is essential to provide appropriate training for inspectors, specialists for inspection teams, and regulatory consistency within the Agency. Accordingly, a Special Assistant to the Commissioner for Biotechnology will be appointed whose charge will be to review current programs, identify areas for research, coordinate the advisory system for product approval within FDA, facilitate training of field personnel, and recommend to the Commissioner appropriate facilities, equipment and personnel to meet the mission of FDA. The Special Assistant for Biotechnology will also coordinate collaborative extramural programs with universities as required.

- **MICROELECTRONICS.** The rapid growth of new technology is no more clearly demonstrated than in the field of microelectronics and microprocessors. The field is proliferating out of the laboratory and into hospitals, physicians' offices, and even into the home. The applications for this technology span a wide range of products, particularly medical devices and radiological products. This field is also significant to the FDA in other respects:

  a. it is one where technical expertise is very difficult to recruit and to retain;

  b. it represents disciplines that will be a necessary component of the FDA's mission well into the 21st century;

  c. it is an area where FDA's capabilities, both in terms of human and physical resources, are limited and dispersed; and

  d. it is a field in which FDA must develop and maintain a strong technical capacity to support fulfillment of our regulatory mission.

Accordingly, FDA plans to develop a capability in this area that will place the Agency in a clear position of recognized technical competence and will equip the Agency to regulate this technology effectively. This effort should serve as a model for other scientific programs that will need similar attention in the future.

To achieve this objective, FDA will take the following steps:

1. **RESOURCES.** FDA's Center for Devices and Radiological Health (CDRH) will take steps to establish a state-of-the-art capability in both human and physical resources for microelectronics and microprocessors to ensure that the Agency can successfully meet its regulatory responsibilities for products that employ this technology and for related manufacturing processes.
2. **FIELD CAPABILITIES.** The Office of Regulatory Affairs (ORA) will take steps to enhance further FDA's field capabilities related to the inspection of products and manufacturing processes involving microelectronics and microprocessors. This enhancement will involve further training of field staff in consultation with CDRH.

9. HEALTH FRAUD

- *FDA will implement a significantly broadened initiative aimed at reducing health fraud, including both increased emphasis on enforcement activities and increased efforts at achieving consumer and health professional awareness. Particular attention will be given to focused efforts on health fraud creating health hazards and life threatening dangers.*

For many years the Agency has fought against the promotion for profit of medical remedies known to be false or unproven. Once known as "quackery," health fraud includes serious and direct health hazards and life threatening dangers, as well as strictly economic deception. Because direct health hazards are a clear and immediate danger to public health, FDA has always given them a substantial priority, and has used civil, criminal, and administrative sanctions to remove such products from the market. Other kinds of fraud include indirect health fraud (where a patient delays proper medical treatment or is persuaded to use an ineffective one) and health-related economic fraud (worthless, yet harmless articles promoted to improve health or appearance).

Interest in health fraud among consumers, the medical community, and Congress has increased in recent years, and one Congressional estimate concludes that perhaps $10 billion is wasted each year on fraudulent medical products. Although health fraud is a difficult and pervasive problem that can never be entirely eliminated in a free society, FDA has responded by taking actions that can serve as the beginning of a major new program. FDA's health fraud activities have been elevated to a defined project that can coordinate the exchange of information within and without the Agency, promote cooperative efforts, and establish measures to help determine where increased efforts are most needed. Collaborative agreements have been made with the Better Business Bureau to alert newspapers, magazines, and other mass media to be watchful for fraudulent articles and advertisements; and with the Pharmaceutical Advertising Council to carry out a nationwide public service campaign to warn consumers against health fraud. FDA's Centers have begun to develop programs that focus on medical devices, drugs, foods, and cosmetics that pose health hazards.

These steps are the first in a larger program intended to make health fraud a National concern. Because the Agency's experience has shown that regulatory action against health fraud is most effective when supported by expanded consumer awareness of the problem, FDA will combine its emphasis on enforcing the laws prohibiting fraud with intensified efforts to educate consumers and the health professional community about the nature -- and dangers -- of fraudulent medical and food products.

More specifically, FDA will utilize the following methods:

- **ENFORCEMENT** - FDA's Office of Regulatory Affairs (ORA) will place increased emphasis on enforcement efforts aimed at fraudulent products that pose direct or significant indirect health hazards. ORA will also intensify its search for and take appropriate action against high visibility or widespread fraudulent products that are known to snare large numbers of unknowing consumers.
- **EDUCATION** - FDA's Office of Consumer Affairs (OCA) will coordinate an expanded national awareness of health fraud, particularly regarding specific examples of fraudulent products. In particular, the Agency will focus on consumer education and information programs, thereby coordinating efforts to special target audiences, such as the elderly, women, and minorities, that have frequently been victims of such fraud. FDA will coordinate its efforts

with those of State, local, and other Federal agencies, and with national consumer, health professional, and industry organizations, thereby forging a joint effort in planning and delivering information about the health fraud problem directly to the public.

- **INTERAGENCY COOPERATION.** FDA will strengthen links with the HHS Office of the Inspector General, Federal Trade Commission, U.S. Postal Service, and State and local officials so that information about specific products is properly shared and duplication of enforcement efforts is minimized.

10. INTERNAL MANAGEMENT

- *FDA will make significant improvements in its own internal management, particularly in the areas of career advancement, information systems, laboratory research programs, resource allocation, and science base. Particular attention will be given to the Commissioner's Advancement Program designed to meet the personnel needs of the FDA.*

The task forces charged by the Commissioner on August 15, 1984 developed a large number of recommendations for improved management. Only a few are listed here, but they provide an indication of the scope of management initiatives that will be undertaken. Others will be undertaken as well, even though they are not included in this global plan.

- **COMMISSIONER'S ADVANCEMENT PROGRAM.** Recognizing that personnel is the single most important resource in FDA, the Agency will develop a Commissioner's Advancement Program to serve as an umbrella to advance the careers of employees and the goals of the Agency simultaneously. The program will become an integral part of the annual planning process of the Agency. Such planning will analyze how each unit of the Agency will meet its goals. Particular emphasis will be placed on exchange programs with the scientific community, State and local governments, other Federal agencies, and the private sector to aid FDA in keeping pace with the advancing technology. The plan will be designed to include an Agency-wide effort to meet the changing specialized and technical needs of all FDA employees -- secretaries, scientists, regulatory review personnel, and administrative personnel -- in all job categories at all grade levels. Incentives will be integrated into the overall personnel programs. While decentralized in implementation, the coordinated program will be designed and monitored within the Office of the Commissioner, with special support from the Deputy Commissioner in his role as chief operating officer of the Agency.

- **INFORMATION SYSTEMS.** Recognizing the need for a coordinated, efficient information management system, the position of Director of Information Resources Management will be created, supported by the necessary staff for implementation. The new Director will be charged with: identifying and defining existing information needs on an Agency-wide basis; developing standards and reducing redundant requirements by each Center for information from the same industries; drafting guidelines for the use of information systems and ensuring security of information; and analyzing product review and postmarket surveillance information management needs. Particular attention will be directed to information networking and the balance of centralized and decentralized functions.
- **RESOURCE ALLOCATION.** Recognizing the need to manage scarce resources prudently, the Agency will initiate an analysis of several of its current administrative practices, such as lease/purchase practices, laboratory supply purchasing, and maintenance contract policies. Particular attention will be directed to the organization of field activities and to headquarters efforts that will promote appropriate sharing and lead to increased efficiencies. The goal will be to develop a long-range planning process that will enable the Agency to effectively establish priorities among competing programs, and consolidate activities that previously involved duplication of effort.
- **SCIENTIFIC BASE.** Recognizing that the Agency is dependent upon the maintenance of a strong scientific program, a number of science-related management initiatives will be undertaken. To attract and maintain scientists,

career ladders for scientists will be evaluated with particular attention directed at the adequacy of laboratory resources, recognition of outstanding research, and the establishment of a peer review system for intramural research scientists. Particular emphasis will be directed toward cooperative FDA-university interaction, "mini" leaves of absence for scientific and medical personnel as a function of duration of service and career plans, collaborative research, and interchange between field and headquarters scientists. A small competitive Commissioner's travel fund will be established, by reallocating existing resources, to enable outstanding scientists and medical officers to present data at national meetings.

- **INTEGRATED RESEARCH PLAN.** FDA currently carries out research and testing in the areas of risk assessment, human food safety, and related areas in the Center for Food Safety and Applied Nutrition (CFSAN), National Center for Toxicological Research (NCTR), Center for Veterinary Medicine (CVM), and field laboratories (ORA). Although decentralization along product lines has been utilized in the past to ensure that research is designed to support program activity, such decentralization has often lead to criticism that our various research organizations do not work sufficiently close together, and that they sometimes even duplicate each other's work. To address this problem, FDA will be developing a joint CFSAN-NCTR-CVM-ORA research plan for all laboratory activities. This will include: inventorying current laboratory activities; sharing information on current activities and resources; sharing research initiatives and results; establishing effective means of communication across product lines; and setting priorities for future laboratory activities and ensuring that toxicological research and data bases are fully shared. This plan should be developed in conjunction with the risk assessment initiative described earlier in this Action Plan.

- **FACILITIES.** A facilities plan will be developed for the entire Agency that will concentrate both on field and on headquarters needs. Particular attention will be devoted to natural linkages in our facilities design, such as the interrelationship with USDA through the establishment of Modules I and II at the Beltsville campus, our traditional close interrelationship with NIH, and the appropriate cooperation of field laboratories to meet regulatory and research needs. This master plan will provide a mechanism for cost-benefit analysis of geographic location and consolidation of activities within appropriate field facilities and appropriate headquarters facilities.
- **REGULATION DEVELOPMENT.** Recognizing the need to implement regulatory and policy decisions efficiently, FDA will take appropriate steps for ensuring that its regulations are completed in a timely fashion. These steps will include both the establishment of improved coordination procedures within FDA and the development of a team approach in the review of FDA regulations beyond the Agency level. The Commissioner will be responsible for ensuring an expeditious review of regulations. Additionally, FDA will ensure that a full range of options such as education and voluntary efforts are explored before development of a new regulation is undertaken. Enforcement plans will also be developed for each regulatory initiative concurrent with formulation of a new regulation.
- **SPECIAL TARGET AUDIENCES.** The Agency will also be examining crosscutting issues that affect the health of specific target audiences such as women, the elderly, minorities, and the handicapped. FDA will seek to give increased

emphasis to effective ways of communicating important health protection messages, developing specially-designed education programs, and involving these constituents in FDA public participation activities. Programs and actions addressing the needs of some of these groups have already been initiated; for example, FDA has established an internal advisory group on women's health issues to assure that subjects having an important impact on the health of women of all ages are considered in Agency decisions. Furthermore, FDA will sponsor a conference on women's health issues to expand its communication, information, and participation activities with women.

CONCLUSION

The priorities established in this plan are designed to respond to the Secretary's charge to prepare FDA for the challenges of today and of the 21st century. The Policy Board was deeply impressed by the thoughtfulness both of the Pathway A and of the Pathway B deliberations. Although many of the over 200 Pathway A recommendations could not specifically be discussed in this global plan, all are being carefully evaluated and implemented as appropriate. The members of the Pathway A Task Forces are listed in Appendix II. The categories of Pathway A recommendations are summarized in Appendix III. FDA also learned a great deal from the Pathway B meetings. Accordingly, the Agency will seek to expand and strengthen forums for conducting frequent and open communications with a wide range of constituent groups, including consumers, health professionals, academia, State and local health officials, and members of the regulated industry. A summary of the Pathway B meetings is contained in Appendix IV. The Agency believes that this planning process has generated a feeling of renewal within FDA that will serve to make an already-strong Agency considerably stronger in the years that lie ahead.

APPENDIX I

THE ACTION PLAN DEVELOPMENT PROCESS

This Action Plan is the result of a rigorous and systematic process that was designed to assure the greatest possible participation both of Agency personnel and of important outside constituencies. The process reflected an effort to have the Agency profit from the best ideas of its top-level managers, mid-level staff, and the outside groups with which FDA routinely interacts. Particularly important was the analysis by previous Commissioners of their unfinished agendas. The combined efforts of these individuals and groups have made it possible for the Commissioner and the Agency to respond to Secretary Heckler's charge of preparing the Agency for today and for the 21st century.

INITIATION OF THE PROCESS

The formulation of Action Plan initiatives began in late July 1984, when the Commissioner asked the Policy Board (the Agency's top management team) to articulate what they believed to be the highest priority issues -- areas of Agency activity that would warrant special attention -- as FDA begins to prepare for the future. Members were asked to recommend priorities for the entire Agency, in addition to their particular areas of responsibility. The Policy Board's submission of written comments to the Commissioner was followed by a special evening meeting that was held in early August to focus on choosing several "umbrella" topics for organizing the development of action plans. The result of this session was a list of six themes, or broad categories of Agency activity, to be used as a basis for soliciting suggestions from the Agency for specific initiatives. These six themes were: personnel, resource allocation, information management, scientific base, facilities, and regulatory approaches.

ACTION PLAN TEAMS

The next step in the planning process was the formation of action plan teams to make in-depth analyses of the six broad categories and give recommendations for specific initiatives to be included in the Action Plan. Team members were nominated by the Policy Board to serve on the Action Plan teams; the final selection was made by the Commissioner and Deputy Commissioner with the goal of including people from a wide spectrum of professional disciplines and levels of responsibility within the Agency. Fifty-nine people served on the action plan teams representing all of the FDA centers, the field organization, and many staff offices. Members of the teams had personal expertise in the action plan area to which they were assigned and represented widely varying disciplines and areas of professional responsibility, including regulatory policy development, field operations, product approval, scientific investigation, financial and program management, personnel, information management, and other legal and administrative support activities. This broad-based group provided fertile ground for the generation of wide-ranging recommendations and creative solutions to the challenges of the future.

The action plan teams followed an intensive schedule of activity that culminated in the completion of six reports which were submitted to the Commissioner in early September. Many meetings were held and considerable individual effort expended to formulate the recommendations and supporting data that were incorporated into six reports. The Commissioner contributed to the action team effort by periodically meeting with each team to offer guidance, support, and encouragement.

REVIEW AND CONSOLIDATION OF ACTION TEAM RECOMMENDATIONS

After the completion of the action plan teams' work, the Policy Board undertook the task of reviewing the extensive recommendations and suggestions for future improvement contained in the team reports. Each report was reviewed in depth by a three-person subgroup of the Policy Board. Many of these groups met with members of the action plan teams to further clarify and develop the recommendations. After a thorough review of the reports, the subgroups combined some recommendations, made some additional recommendations, and made suggestions regarding the relative priority of the initiatives suggested by the action teams. The full Policy Board was subsequently reconvened to discuss the conclusions of each subgroup.

The process to this point yielded more than 200 recommended initiatives, including the action plan teams' recommendations, suggestions by the Policy Board subgroups, recommendations made during the full Policy Board session, and written comments submitted by the Policy Board after the special session.

The activities above have been referred to within the Agency as "Pathway A" -- the internal analysis and discussion of priorities for the future. Shortly after the Pathway A activities were started, a second avenue of information gathering was initiated. "Pathway B" activities were designed to collect the insights and suggestions of FDA's varied outside constituencies.

PATHWAY B--COMMENTS FROM OUTSIDE GROUPS

Pathway B gave the Commissioner and other Agency managers the opportunity to gain direct advice from important outside groups for consideration as the Agency formulated its Action Plan. This additional perspective was gained through meetings with representatives of regulated industry, academia, the scientific community, health professionals, consumers, and other Federal, State and local public health agencies. The Commissioner and other Agency executives held 19 meetings with 54 organizations or institutions for this purpose. Different Policy Board members and Chairpersons of the Internal Task Forces accompanied the Commissioner on each Pathway B meeting. One special group was convened to give unique insights on the Agency's activities: in a single meeting, the Secretary, the Commissioner, and other Agency staff met with four of the five previous FDA Commissioners who have led the Agency during the past 15 years.

Before each of the Pathway B meetings, the outside groups were sent a list of questions that had been formulated by the Center Directors and Commissioner's staff. Group representatives responded to these questions during the discussions as well as giving general comments on Agency activities. Many groups also sent the Commissioner written comments.

FINAL FORMULATION OF THE ACTION PLAN

The recommendations, insights, and priorities established during the completion of Pathway A and Pathway B have been synthesized by the Agency and assimilated into the final Action Plan. As individual aspects of the plan's initiatives began to become more focused, the Commissioner met with many of the Center Directors and Associate Commissioners individually. This dialogue helped to clarify the Action Plan objectives and to gain the commitment of the Agency managers in pursuing these objectives.

The final plan represents a synthesis of data, perceptions, experience and advice from virtually every organization and group, inside and outside the Agency, which has an interest in the Agency's continued successful performance. It is a global approach to the issues facing the Agency as it prepares for the 21st century.

APPENDIX II

PATHWAY A PARTICIPANTS: ACTION PLAN TEAMS

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Thomas Scarlett, Esquire
General Counsel

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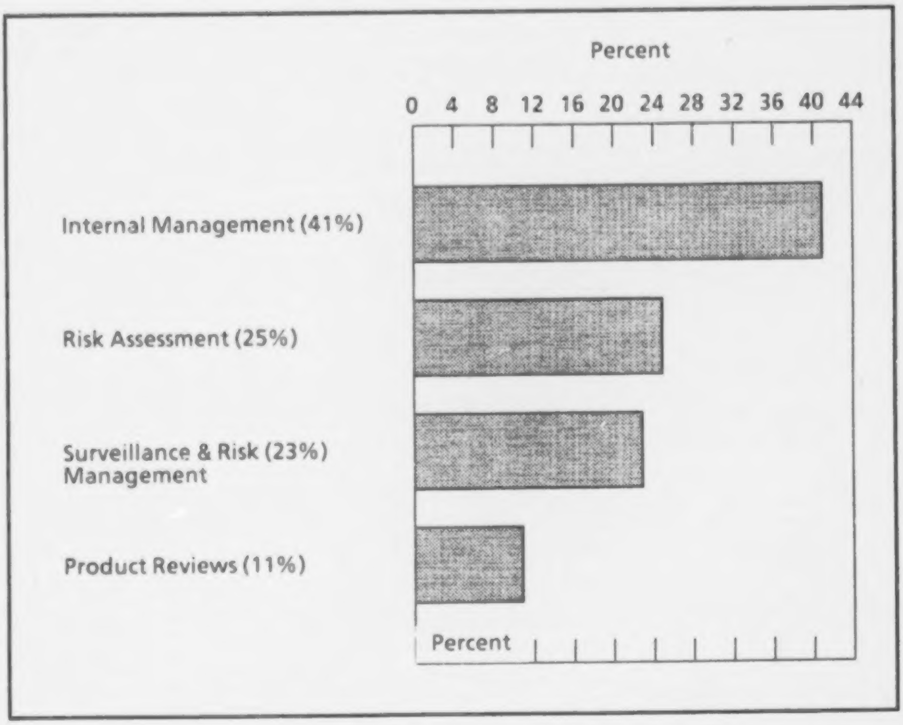
PATHWAY A RECOMMENDATIONS

(Each Type Recommendation as a Percent of the Total)



APPENDIX IV

PATHWAY B PARTICIPANTS

Organization	Meeting Date
Grocery Manufacturers Association	September 7, 1984
National Pharmaceutical Council	September 13, 1984
Pharmaceutical Manufacturers Association	October 4, 1984
Food and Drug Law Institute	October 17, 1984
Health Research Group	October 18, 1984
American Veterinary Medical Association	October 19, 1984
American Medical Association Association of Academic Health Centers Association of American Medical Colleges	October 23, 1984
National Soft Drink Association Food Marketing Institute	October 25, 1984
Association of Minority Health Professions Schools	October 25, 1984
Health Professionals	October 25, 1984

American Society of Hospital Pharmacists
National Association of Chain Drug Stores, Inc.
American Association of Colleges of Pharmacy
American Academy of Opthalmology
American Optometric Association
American Dental Association
American Academy of Family Physicians
United States Pharmacopeia
American Pharmaceutical Association
American Lung Association
National Health Council
American Association of Blood Banks
American Heart Association
American College of Cardiology
American Association for Respiratory Therapy

Organization	**Meeting Date**
Animal Health Institute	October 26, 1984
American Feed Manufacturers Association	October 26, 1984
National Food Processors Association	October 31, 1984
Health Industries Manufacturers Association	November 1, 1984
American Society for Microbiology Federation of American Societies for Experimental Biology	November 2, 1984
University of Maryland Johns Hopkins University	November 2, 1984
Consumer Groups	November 2, 1984
Center for Science in the Public Interest	
Public Voice for Food and Health Policy	
Washington Office Consumers Union	
American Association of Retired Persons	
Community Nutrition Institute	
Department of Consumer Education and Resource Management - Howard University	
National Council of Negro Women	
National Women's Health Network	
Public Citizen Litigation Group	
Swankin and Turner	
George Washington University Law Center	
State Officials	November 27, 1984
Association of Food and Drug Officials	
National Association of State Departments of Agriculture	
Association of American Feed Control Officials	
Association of State and Territorial Health Officers	
National Association of State Boards of Pharmacy	
Association of American Pesticide Control Officials	
University of Arkansas	Via telephone conference

APPENDIX 4

NIH Program Evaluation Report

AN ANALYSIS OF RESEARCH PUBLICATIONS SUPPORTED BY NIH 1973-76 and 1977-80

National Institutes of Health
and
NIH Intramural Program

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ANALYSIS OF PUBLICATIONS ON NIH-SUPPORTED RESEARCH 1973-76 and 1977-80

NIH--All Institutes Combined and the Intramural Program

INTRODUCTION: THE BID-MEDLINE PUBLICATION DATA SET

This report presents an analytic characterization of the 1973-80 biomedical research publications supported by the National Institutes of Health. Part I describes NIH publications for the intramural and extramural research programs combined; Part II focuses on intramural research publications only. Parallel analyses have been conducted for each of the Bureaus, Institutes, and Divisions (BIDs), and a report on each Institute is available.

Since 1973, CHI Research, the research group at Computer Horizons, Inc., has worked under contract to NIH (contracts N01-OD-3-2109 and N01-OD-1-2109) on the development and application of indicators of biomedical research activity. The present reports are a product of this collaborative association.

These reports supersede the previous set of bibliometric evaluation reports covering the period 1970-76 (11). It should be noted that the first set contained no report for the total NIH--all Institutes combined--or for the intramural research program. The reader should also be aware that the reports for the individual Institutes from these two sets are not strictly comparable. Partly because of changes in MEDLINE journal coverage, and partly because the Institute for Scientific Information has shifted most behavioral science journals from the Science Citation Index (SCI) to the Social Science Citation Index, the present set of reports is limited to coverage of clinical medicine and biomedical research. Chemistry and psychology, which were covered in the previous set of reports, are not included in the computer-generated data of this set. Paper counts obtained manually, however, were used in certain calculations, as noted below.

The present set provides a comparative analysis of the papers published in a selected group of 240 biomedical journals for two time frames--1973-76 and 1977-80. The 240-journal set contains, overall, about 75 percent of the NIH-supported research papers published during this period. These 240 journals are designated as the "BID-MEDLINE journal set." Limitation of the analysis to this subset of journals was due to the necessity of examining each paper individually to determine sources of support. Beginning, however, with the publication year 1981, inclusion of data on support acknowledgement in the National Library of Medicine's MEDLINE system, which covers about 2,000 biomedical journals, has made possible more extended and refined analyses.

Journal Selection

The information contained here is drawn from an analysis of some 460,000 papers published between 1973 and 1980 in 240 biomedical research journals. The publications attributed to a given Institute report on both intramural and extramural (grant- and contract-supported) research.

The need to examine each paper for acknowledgement of support dictated restriction of the study to a limited number of journals. The initial selection aimed at:

- Representing all biomedical research areas by their most influential (most often cited) journals, and

- Covering as many of the papers supported by NIH as possible.

Through selection of the most influential journals and those that maximize coverage of NIH-supported papers, the role of NIH in bioscience publication is somewhat magnified. Future reports, which will be based on all MEDLINE/SCI-covered journals, will include many in which NIH-supported authors publish less frequently. The NIH presence in these collective fields and subfields will be smaller.

Previous reports on these bibliometric studies were based on papers in 275 journals covered by the SCI. During the evolution of the present project, it was decided to merge the set with the MEDLINE data base of the National Library of Medicine. This resulted in a more limited data set, for the process of merging excluded journals not common to the two component systems. The new "BID-MEDLINE journal set contains 240 journals.

These are listed by subfield in Appendix C. Because MEDLINE has limited its coverage of Chemistry in recent years, and neither SCI nor MEDLINE offers more than minimal coverage of the behavioral sciences, these two fields are underrepresented in the present studies.

Data Capture

Development of the BID-MEDLINE data set required that every paper published in the original 275 journals between 1970 and 1980 be scanned to capture acknowledgements of BID support. Up to three acknowledgements are tabulated and added to the original listings drawn from the SCI. When more than one source of support is acknowledged, fractional credits are assigned. For example, a paper acknowledging both NCI and NIAID is counted as one-half paper for each Institute. The resulting lists are then matched to SCI corporate tapes to obtain author institutional affiliations. Up to three affiliations are entered in the data set.

The final step in the development of the 240-journal data base requires matching the papers in the 275 SCI journals to the MEDLINE data base. This match provides titles of the papers, names of all authors, and medical subject headings (MeSH: index terms). The product of this match constitutes the 240-journal BID-MEDLINE data base, 1970-80.

Representativeness of the Data

Adequacy of coverage of the original 275-journal set was assessed principally by comparing the number of BID-supported papers found in these journals with the numbers reported in the 1973 NIH Research Grants Index and the NIH Directory-Bibliography. In making these comparisons, books, abstracts, and other inappropriate (for this purpose) items were not counted. Overall, the selected group of 275 journals contained approximately 80 percent of all NIH-supported papers.

The adequacy of the journal set was also assessed by correlating the number of papers in each biomedical subfield in the BID set with the number of U.S. papers in the same subfields in the over 900 biomedical journals in the Science Citation Index (SCI). Correlation of the two sets was .98.

NIH Support of Research in Chemistry and Psychology

Although the unavailability of Chemistry papers in MEDLINE and of most Psychology papers in both SCI and MEDLINE precludes coverage of these fields in the computer-generated tables in this report, some data are available. For the field of Chemistry, information on source of support has been obtained manually for the entire report period, 1973-76 and 1977-80. Psychology data are available through 1976. These data have been used in correlating Institute funding with research publications.

Table 1 shows the number and percent of each BID's supported papers in the original 275-BID-journal set for (a) Chemistry for the periods 1973-76 and 1977-80 and (b) Psychology for 1970-76.

Obviously, the loss of coverage of the field of Chemistry has an important effect on the adequacy with which the publication performance of NIGMS can be described. With 12 percent of the Institute's publications omitted, all such statistics as the activity index, percent of internal effort, and citation rates are somewhat distorted. While the effects on NCI and NIADDK data are substantial, their summary statistics should not be significantly affected.

Similarly, the loss of coverage of the Psychology literature deprives NICHD of important program information and significantly affects other NICHD publication statistics. Although we have no data after 1976 on reports of psychological research, we can assume that at least NICHD and NIA performance records are underrepresented in the present data sets.

Journal Coverage

One of the limitations of basing analyses on a fixed set of journals is the possibility that substantive growth of a discipline may result in

Table 1

NUMBER AND PERCENT OF NIH-SUPPORTED PAPERS ON
CHEMISTRY (1973-76 AND 1977-80)
AND PSYCHOLOGY (1970-76) IN 275 JOURNALS

	Chemistry				Psychology	
	1973-76		1977-80		1970-76	
	Number	Percent*	Number	Percent*	Number	Percent*
NCI	809	6.6%	1,031	7.0%	6	0.1%
NEI	17	0.9	21	0.9	89	3.1
NHLBI	197	2.1	244	2.3	33	0.2
NIA**	0	0.0	5	1.2	5	7.6
NIADDK	378	3.9	284	3.0	35	0.2
NIAID	101	1.7	118	2.2	4	0.1
NICHD	56	1.1	42	0.9	1,075	12.7
NIDR	30	2.0	30	2.2	23	0.9
NIEHS	Not determined		Not determined		Not determined	
NIGMS	1,031	10.9	1,191	12.2	117	0.7
NINCDS	91	1.6	59	1.1	416	4.1

---

*Percent of Institute's papers that are in this field.

**NIA-supported papers first appeared in 1975.

substantial change in journal utilization. For example, new journals may draw off many authors in a rapidly growing specialty area. Such changes can be expected to affect BID records differentially and cannot be measured with a fixed set of journals.

A special study (13) was made during the past year to assess the significance of this kind of problem. Two subfields, Endocrinology and Immunology, were selected for study. They were chosen for different reasons and were expected to produce different results. Immunology was selected because it was thought to be a candidate for rapid advance in new directions that might result in new journals and changing patterns of journal utilization. Endocrinology was selected because it was perceived as not having changed dramatically in types of research activity in recent years, and hence as not likely to exhibit marked changes in publication patterns.

All 1975 and 1980 papers in SCI-covered journals in the two subfields were manually examined for research support acknowledgements. The results were compared with the figures obtained from the corresponding subfields in the 240 BID-MEDLINE journal set. (The 240 journal set covers 7 of 24 SCI-covered Endocrinology journals and 9 of 36 SCI-covered Immunology journals.) Results for the two subfields contrast sharply.

Percent of NIH-Supported Papers in
Two Subfields of the BID-MEDLINE 240-Journal Set

	Endocrinology	Immunology
1975	81.1	65.9
1980	82.2	58.5

Although the 7 Endocrinology journals in the 240-journal set include only 56 percent of all Endocrinology papers, they publish over 80 percent of NIH-supported papers in this field. For almost all BIDs, these 7 journals captured 80 to 87 percent of the acknowledgements of NIH research support in both 1975 and 1980. Only NHLBI Endocrinology research is less well captured (70 percent in 1975 and 64 percent in 1980). Overall, it is apparent that reports based on the 240-journal set provide accurate intra-NIH comparison information but overestimate the role of NIH in national or international comparisons.

With respect to Immunology, however, our concerns about extent of coverage proved well founded. The extensions of this field are not well reflected in the 9 Immunology journals in our 240-journal set. For example, while NCI-supported investigators produced 57 percent more Immunology papers in 1980 than in 1975, the 240-journal set shows only a 39 percent increase. NIAID investigators produced 12 percent more Immunology papers in 1980, but the 240-journal set shows nearly a 1 percent reduction in the number of supported papers.

Overall, the Immunology journals in our set captured 66 percent of NIH-supported research in 1975, but only 58.5 percent of the NIH papers published in 1980. While 70 percent of NIADDK-supported papers appeared in the 9 journals in 1980, only 56 percent of NHLBI and 58 percent of NIAID-supported papers appeared there. Data on Immunology publication must therefore be interpreted cautiously.

Citation Frequency

The number of times each paper in the data set was cited has been added to the data base, utilizing the SCI citation tapes for 1973 to 1980. In the citation matching, BID and institutional identifications as well as MEDLINE data have been retained for both references and citations.

Field Coverage

CHI Research has assigned all SCI-covered journals to one of nine major fields of science:

Clinical Medicine	(1)
Biomedical Research	(2)
Biology	(3)
Chemistry	(4)
Physics	(5)
Earth & Space Science	(6)
Engineering & Technology	(7)
Psychology	(8)
Mathematics	(9)

Since the 240 BID-MEDLINE journals primarily publish reports of clinical medicine and biomedical research (Fields 1 and 2), the following analyses are restricted to these two areas. Ninety-four percent of the papers in these journals are in the two fields.

Subject and Level Classification

A journal classification system has been developed in which each biomedical journal is assigned to 1 of 46 biomedical subfields.* The 46 subfields are also collectively grouped into clinical medicine or biomedical (basic) research. The journal classification thus permits characterization of each BID's research support activity into journal-defined traditional disciplines, such as Physiology, Microbiology, Immunology, and Pathology. These subfields are listed in Table 2.

Journals have also been assigned to a "research level." The level concept assumes the existence of a scale ranging from clinical observation (Level 1) to basic science (Level 4) journals. The level designations and a "prototype journal" for each level are as follows:

Level 1 - Clinical Observation. Prototype: *Journal of the American Medical Association*

Level 2 - Clinical Mix. Prototype: *New England Journal of Medicine*

Level 3 - Clinical Investigation. Prototype: *Journal of Clinical Investigation*

Level 4 - Basic Research. Prototype: *Journal of Biological Chemistry*

Classification by level affords a useful perspective for consideration of BID programs. The classification system is described in greater detail in references 1 and 2. Additional clarification of the concept may be obtained by reviewing the level assignment of each of the journals in the 240-journal set (Appendix C).

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*A few multidisciplinary journals (e.g., *Science*, *Nature*, *Proc. Nat. Acad. Sci.*) have been split--i.e., fractionally assigned to more than one subfield.

Table 2

Field and Subfield Classification of Publications

Clinical Medicine

- General & Internal Medicine
- Allergy
- Anesthesiology
- Cancer
- Cardiovascular System
- Dentistry
- Dermatology & Venereal Diseases
- Endocrinology
- Fertility
- Gastroenterology
- Geriatrics
- Hematology
- Immunology
- Obstetrics & Gynecology
- Neurology & Neurosurgery
- Ophthalmology
- Orthopedics
- Arthritis & Rheumatism
- Otorhinolaryngology
- Pathology
- Pediatrics
- Pharmacology
- Pharmacy
- Psychiatry
- Radiology & Nuclear Medicine
- Respiratory System
- Surgery
- Tropical Medicine
- Urology
- Nephrology
- Veterinary Medicine
- Hygiene & Public Health

Biomedical Research

- Physiology
- Anatomy & Morphology
- Embryology
- Genetics & Heredity
- Nutrition & Dietetics
- Biochemistry & Molecular Biology
- Biophysics
- Cell Biology, Cytology & Histology
- Microbiology
- Virology
- Parasitology
- Biomedical Engineering
- Miscellaneous Biomedical Research
- General Biomedical Research

PART I. TOTAL NIH

NIH FUNDING AND PUBLICATION TRENDS

Figures 1 through 5 summarize trends in funding and publication for NIH overall, for each of the Institutes, and for the entire BIO-MEDLINE data base.

Figure 1 depicts NIH obligations from 1965 through 1980, in constant (1969) dollars.* Between 1970 and 1980, total NIH obligations in constant dollars increased by 62 percent.

Figure 2 shows all NIH papers, Fields 1-9 in the BIO-MEDLINE data set for 1970 through 1980. Also shown are the remaining U.S.-authored and -supported papers in this data set. Between 1970 and 1980 the total NIH-supported papers increased 30 percent, while Other U.S. declined 13 percent (1973-80). Over the decade, total BIO-MEDLINE papers increased 40 percent. Data for 1970-72 U.S. and U.S.-supported papers are not available, so the corresponding change cannot be determined.

Figure 3 summarizes the changes in sources of support for the BIO-MEDLINE papers, Fields 1 and 2, between two periods, 1973-76 and 1977-80. The most notable changes are the relatively large increase in the foreign papers,** from 29.6 percent of all the BIO-MEDLINE papers (Fields 1 and 2) in 1973-76 to 32.9 percent in 1977-80, and the increase from 20.5 to 23.1 in the percent of U.S. papers that acknowledged no support. Although the percent of NIH-supported papers decreased from 29.1 to 28.0, the number of such papers increased.

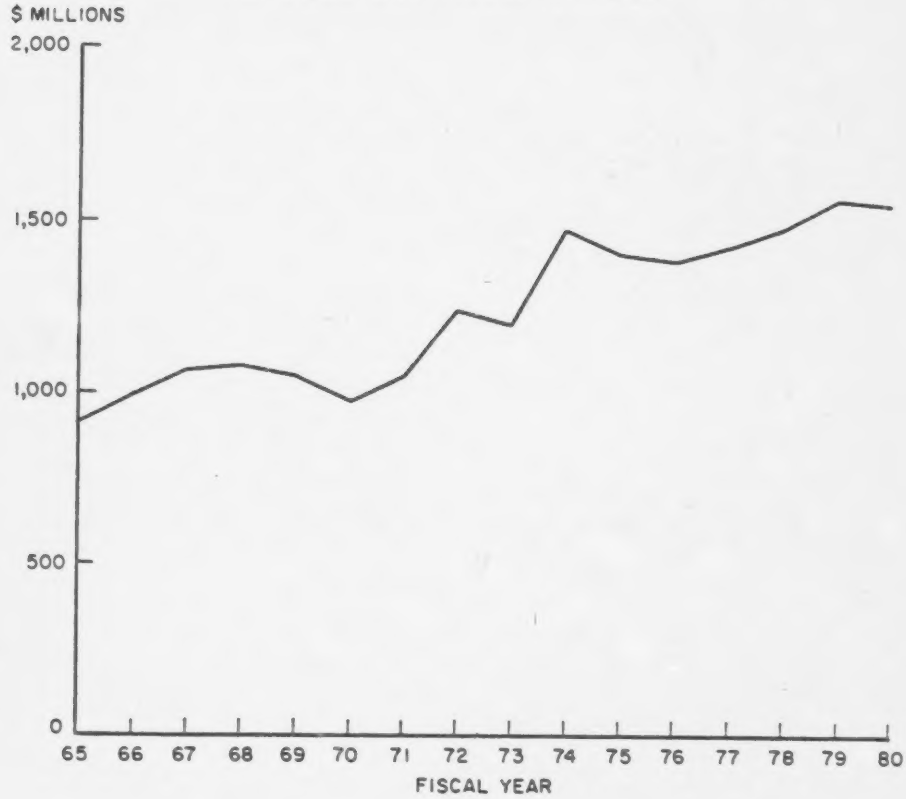
---

*Constant dollar estimates based on NIH Biomedical R&D Price Index.

**Foreign papers are those with foreign institutional authors who are not supported by a U.S. agency. For example, a French scientist's paper acknowledging support from NCI is counted as an NCI-supported paper, not as a foreign paper.

Figure 1

NIH OBLIGATIONS, FISCAL YEARS 1965-1980, IN CONSTANT (1969) DOLLARS*



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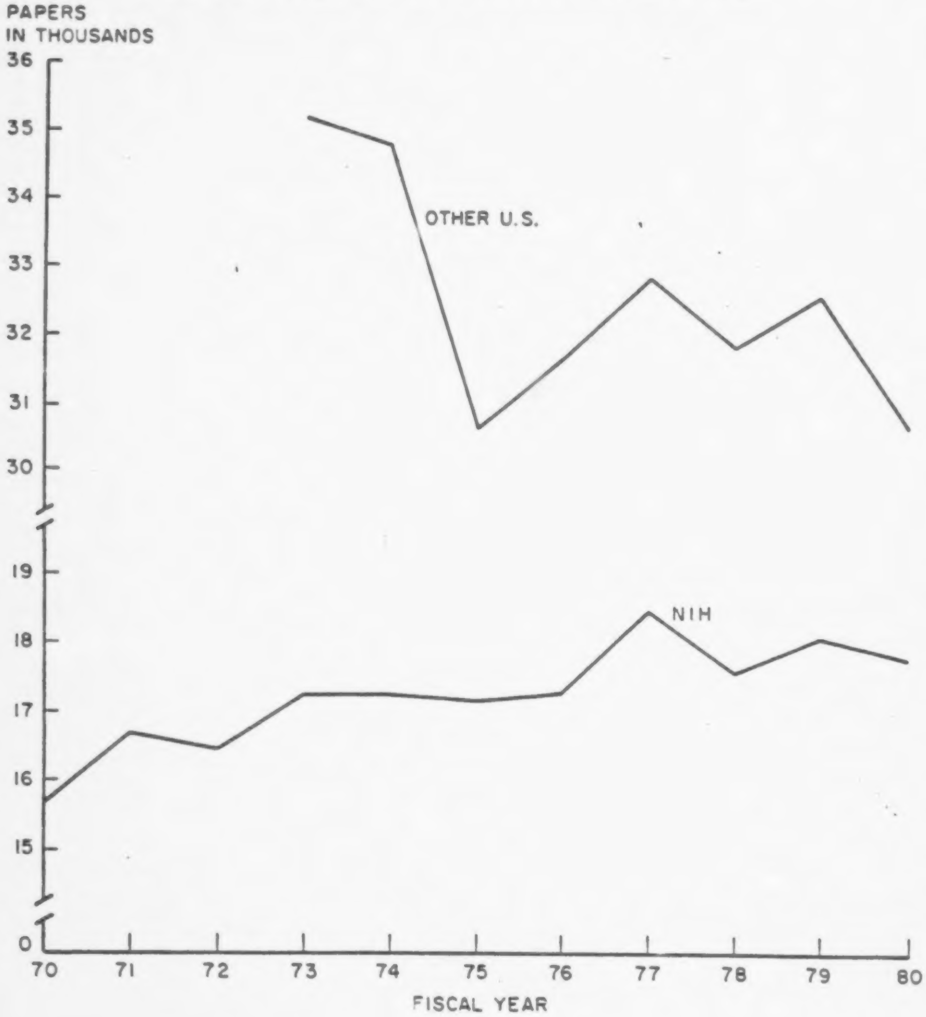
*1965-68 data from "Basic Data Relating to the National Institutes of Health, 1976," p. 15. 1969-80 data from "Basic Data Relating to the National Institutes of Health, 1981," p. 11. NIH Publication No. 81-1261, May 1981. Excludes FIC, NLM, OD, Buildings and Facilities, HRF construction grants, and programs that have been transferred out of NIH. Biomedical Price Index was used to adjust current to constant dollars.

Figure 2

NIH-SUPPORTED AND ALL OTHER U.S.-SUPPORTED PAPERS
BID-SCI JOURNAL SET, FIELDS 1-9, 1970-80*



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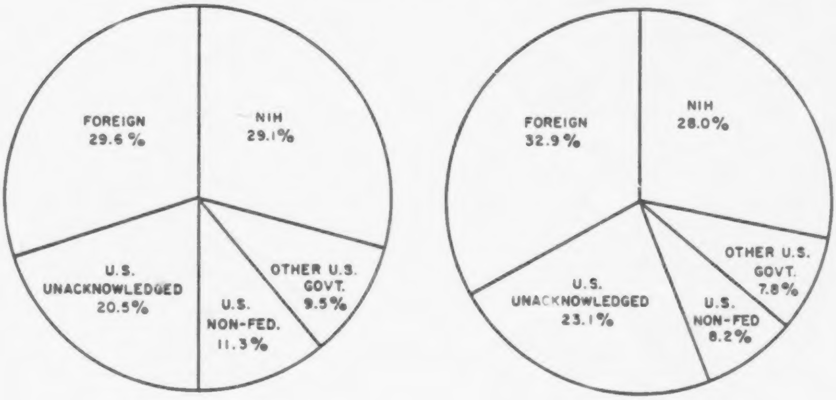
*Data not available on all U.S.-authored and -supported papers for 1970-72.

Figure 3
PERCENT DISTRIBUTION OF BIOMEDICAL RESEARCH PUBLICATIONS BY SOURCE OF SUPPORT, 1973-76 AND 1977-80
(BIO-MEDLINE FIELDS 1 AND 2)



205,922 PAPERS
1973-76

229,375 PAPERS
1977-80

Figures 4 and 5 permit comparison of overall trends in funding and publication for the NIH BIDs covered in this series of evaluation reports.

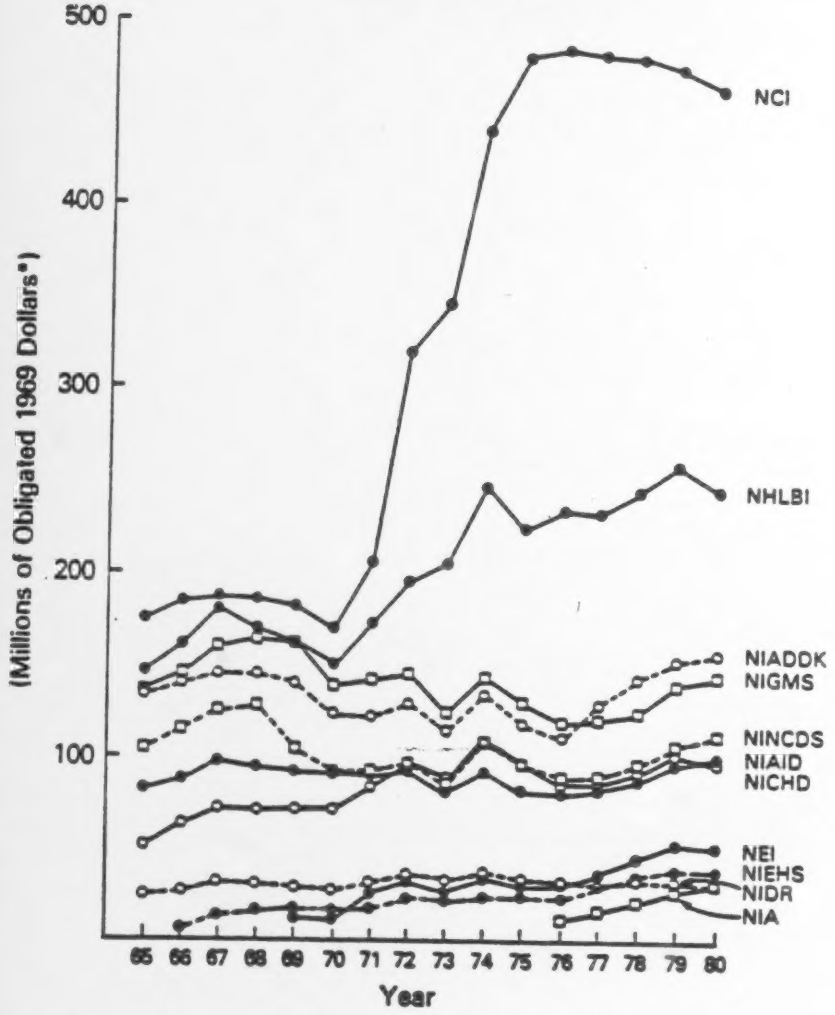
Figure 4 depicts total obligations for each BID, from 1965 through 1980, in 1969 dollars. Between 1970 and 1976, changes in constant-dollar obligations fluctuated for most BIDs. NCI and NHLBI obligations increased greatly; increases were smaller but consistent for NEI and NIEHS. Some BIDs actually declined in financial strength over this period. Between 1976 and 1980, however, obligations in constant dollars increased moderately for all BIDs except NCI and NIDR.

Figure 5 shows corresponding publication trends for the NIH BIDs from 1970 through 1980. Close relations between publications and funding are clearly depicted in the large increase in annual publication rates for NCI and NHLBI and in the manner in which most BIDs range below them. NIADDK and NIGMS appear to be the exceptions. They seem to support a great many more publications than would be expected, given their sizes. The apparent discrepancy occurs because these two institutes support proportionally more basic science research than do other BIDs, and basic scientists on average publish many more papers than do clinicians.

Data are not available to permit discussion of rate of publication per support dollar, etc., nor are they sought. While for NIH as a whole the correlation between funding and publication rate is extremely high ($r = .90$), such relationships may break down when smaller aggregates are analyzed. Characteristic differences between disciplines and classes of disciplines (e.g., clinical vs. basic science), between individual scientists and those working in interdisciplinary groups, among stages of development of subdiscipline specialty areas, etc., may mask a strong underlying relationship. Therefore, when small aggregates of data are the focus of interest, care in analyzing potential covariates is essential.

Figure 4

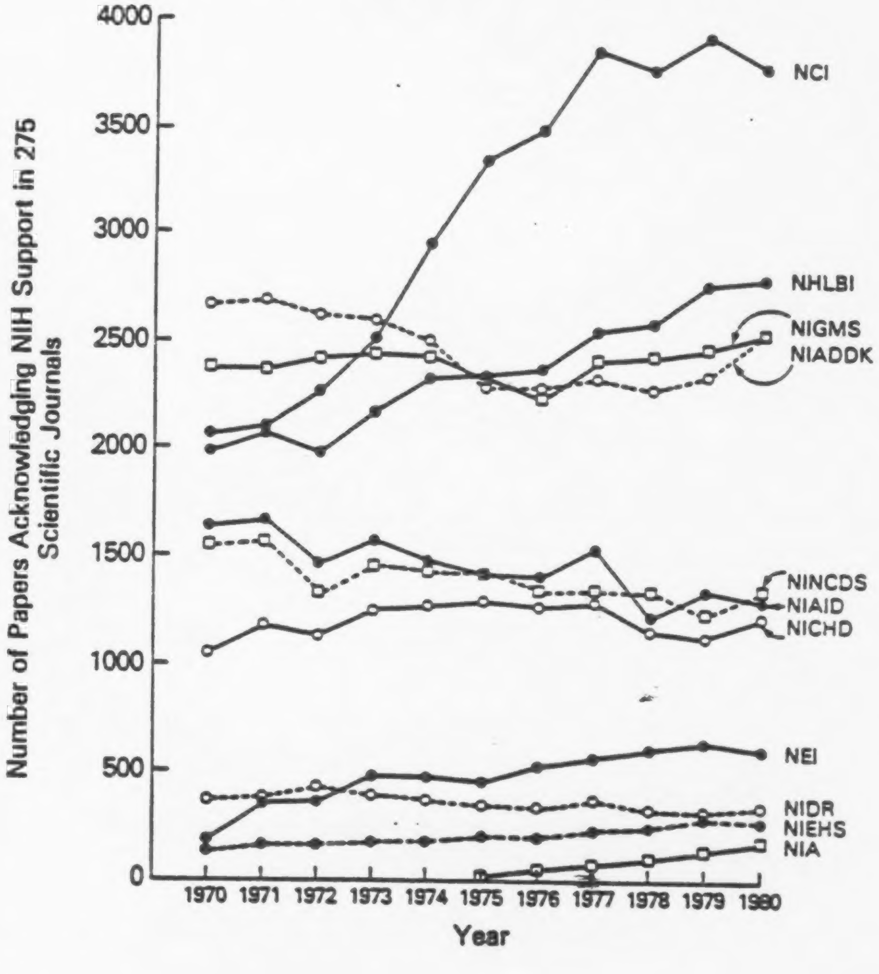
BID Obligations 1965-1980
(1969 Constant Dollars)



*Based on NIH Biomedical R&D Price Index

Figure 5

Acknowledgements of Research Support Appearing in 275 Scientific Journals



Note: The paper counts in this figure are for Fields 1 through 9, but 90 percent of the total papers are in Fields 1 and 2.

NIH PUBLICATION ACTIVITY

The tables and graphs in this section present a detailed bibliometric profile of NIH-supported research in the BIO-MEDLINE journals. Since one goal of this report is to identify changes in NIH-supported research activity, most of the publication profile data are presented for two periods--1973-76 and 1977-80. Research-level and research-field profiles of NIH-supported papers are presented in Tables 3 and 4, and publication profiles relating NIH-supported papers to all BIO-MEDLINE papers by research area are presented in Figures 6A, 6B, 7A, and 7B (constructed directly from data in Tables 5A and 5B).

Research-Level Profile

Table 3 presents the level classification of NIH-supported publications for the two periods 1973-76 and 1977-80. There was a decrease in the number and percent of NIH-supported papers at the more clinical levels (1 and 2) and an increase in number and percent of NIH-supported papers at the more basic levels--Clinical Investigation (Level 3) and Basic Research (Level 4). It should be noted that nearly 80 percent of the NIH-supported papers are at Levels 3 and 4, and that nearly 50 percent are at 4.

Table 3

Number and Percent of All NIH-
Supported Papers in Fields 1 and 2 According to
Research Level, 1973-76 and 1977-80

Level	1973-76		1977-80*	
	Number	Percent	Number	Percent
Levels 1 & 2 (Clinical Observation & Clinical Mix)	14,377	24%	13,786	21%
Level 3 (Clinical Investigation)	18,250	30	19,845	31
Level 4 (Basic Research)	27,316	46	31,279	48
Total	59,943	100%	64,910	100%

---

*1980 data include a 5 percent estimate for 1980 papers appearing on 1981 SCI tapes.

Publication Counts

Figures 6A and B show the percent of all papers in clinical medicine and biomedical research, respectively, in the BID-MEDLINE journal set that were NIH-supported. Publication activity for the two periods 1973-76 and 1977-80 is shown for each subfield. Clinical medicine comprises 32 subfields as defined in the 240-journal set; biomedical research, 14.

NIH supported a substantial number of papers in nearly every subfield. In Cancer and Immunology, NIH supported more than 40 percent of the total 1973-80 BID-MEDLINE papers. It supported more than 30 percent of all papers in seven other subfields of clinical medicine: Allergy, Cardiovascular System, Endocrinology, Hematology, Ophthalmology, Pathology, and Respiratory System.

Among the subfields designated as biomedical research, NIH supported more than 40 percent of all the 1973-80 papers in each of the following: Physiology, Anatomy-Morphology, and Virology. NIH supported more than 30 percent of the total papers in five additional subfields of biomedical research: Embryology, Biochemistry-Molecular Biology, Biophysics, Cell Biology-Cytology-Histology, and Miscellaneous Biomedical Research.

For most subfields the percent of total BID-MEDLINE papers that acknowledged NIH support decreased from the first period, 1973-76, to the second, 1977-80. These decreases occurred in 24 of the 32 subfields of clinical medicine (Figure 6A). The NIH share increased in only four of the clinical subfields. In the more basic subfields (Figure 6B), the NIH-supported proportion decreased in 6 and increased in 5 (of 14). As previously noted, foreign papers increased from 29.6 percent of the total BID-MEDLINE papers (Fields 1 and 2) to 32.9 percent, and the percent of papers that acknowledged no support increased from 20.5 to 23.1 percent (see Figure 3).

Activity Indexes

NIH publication activity is described from another perspective in Figures 7A and 7B, which show the distribution of "activity indexes" for the two periods 1973-76 and 1977-80. The activity index is a ratio of percentages; it is determined by dividing the percent of an Institute's papers in a subfield by the percent of all journal papers in the subfield (as subfields are defined in the BID-MEDLINE journal set). Expressed another way, the graphs display areas in which NIH's publication activity is high relative both to the size of NIH and to the size of the subfield. Thus, an activity index of 1.0 would represent equivalence between the size of the NIH effort in a given subfield and the size of the subfield in the BID-MEDLINE journal set. Activity indexes greater than 1.0 indicate areas of NIH relative emphasis.

The subfields in which NIH had high activity indexes (> 1.4), and had at least 1 percent of its papers, are Cancer, Immunology, Physiology, and Virology.

Figure 6A

Total NIH

Percent of All Papers in Each Subfield of Clinical Medicine Supported by or Performed by NIH

240 BID–MEDLINE Journals

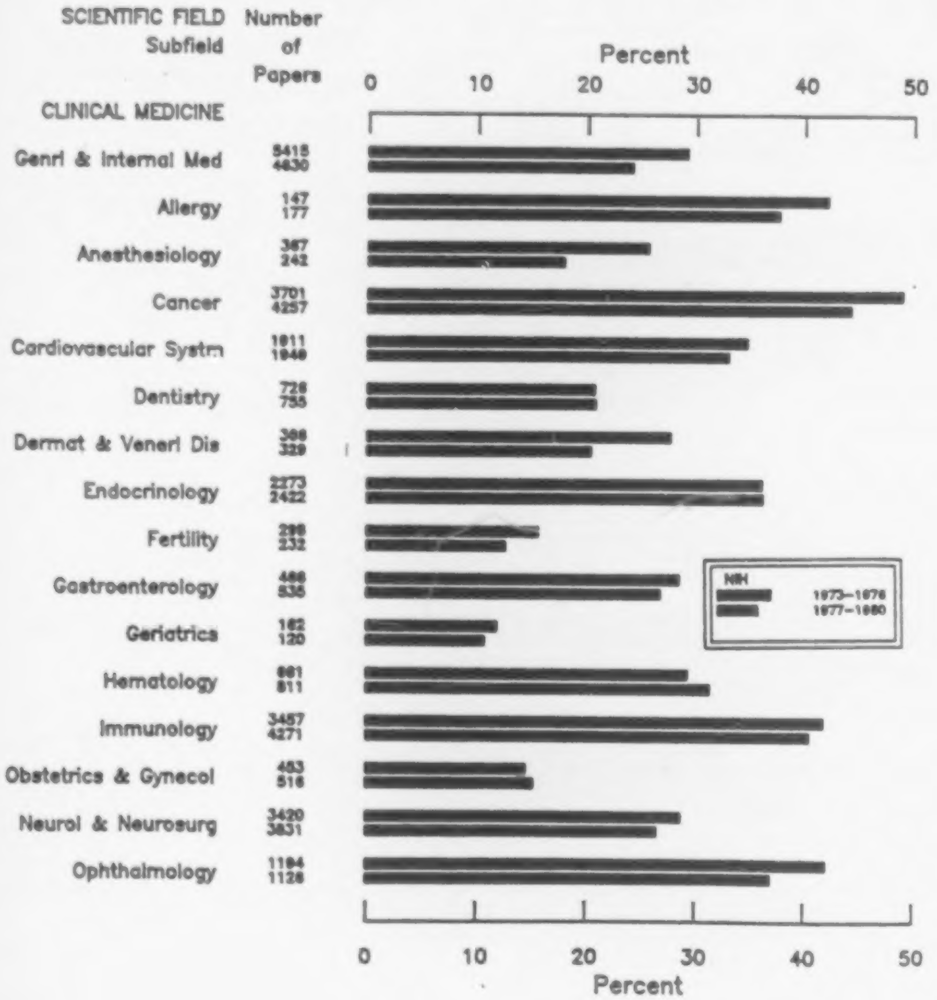


Figure 6A (Continued)

Total NIH

Percent of All Papers in Each Subfield of Clinical Medicine Supported by or Performed by NIH

240 BID-MEDLINE Journals

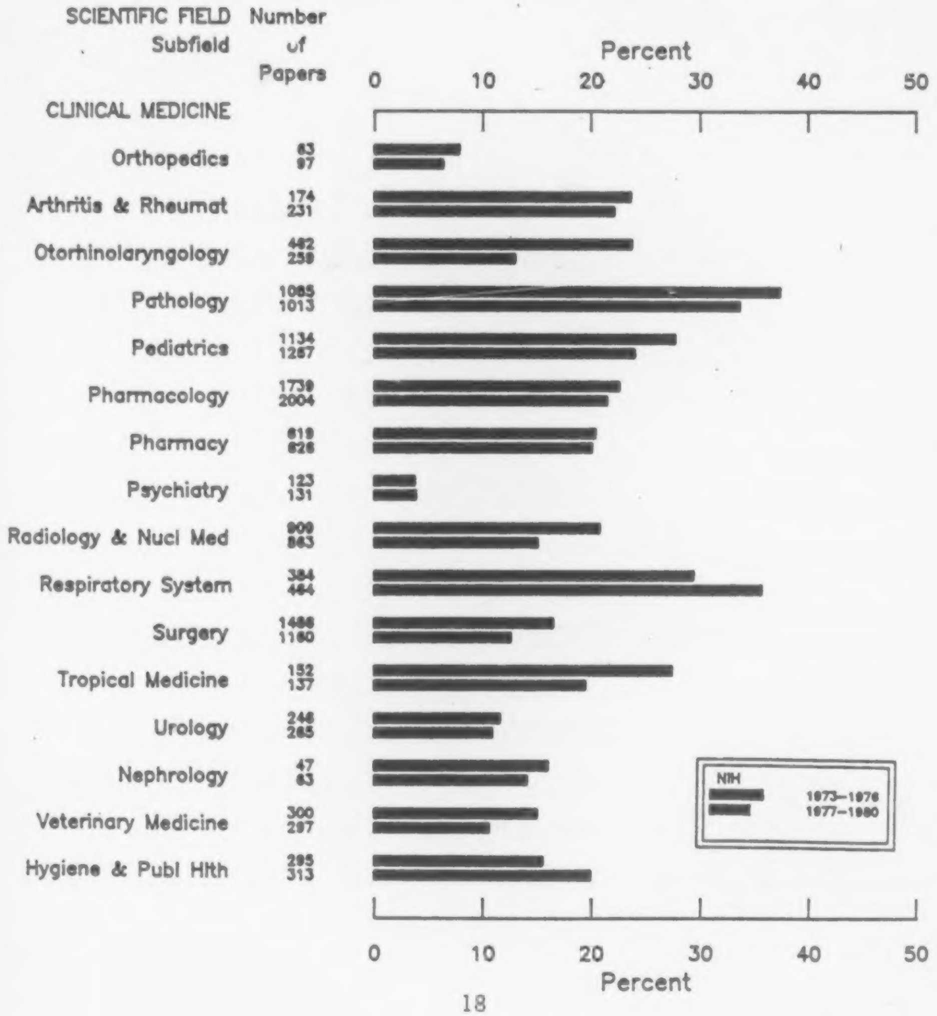


Figure 6B

Total NIH

Percent of All Papers in Each Subfield of Biomedical Research Supported by or Performed by NIH

240 BID—MEDLINE Journals

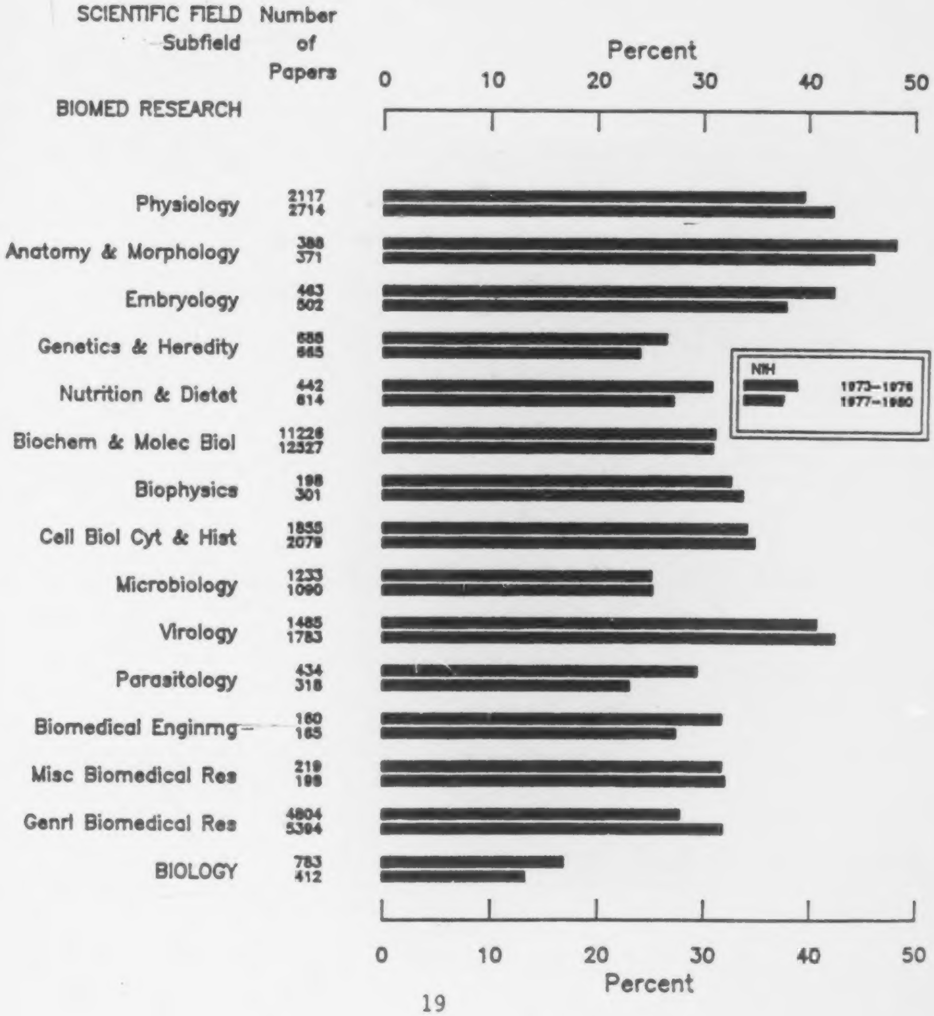
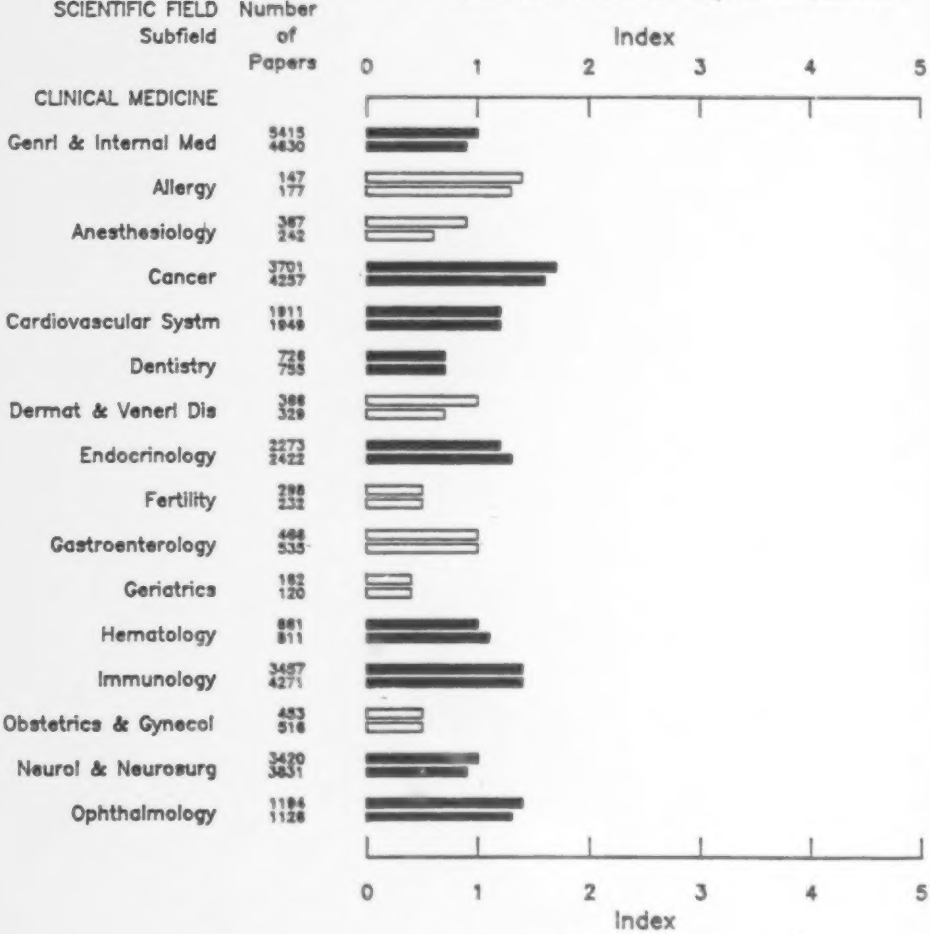


Figure 7A

Total NIH Activity Indexes in Subfields of Clinical Medicine

240 BID–MEDLINE Journals
1973–1976 over 1977–1980

$$\text{INDEX} = \frac{\text{\% of Institute's Papers in Subfield}}{\text{\% of 240 Journals' Papers in Subfield}}$$



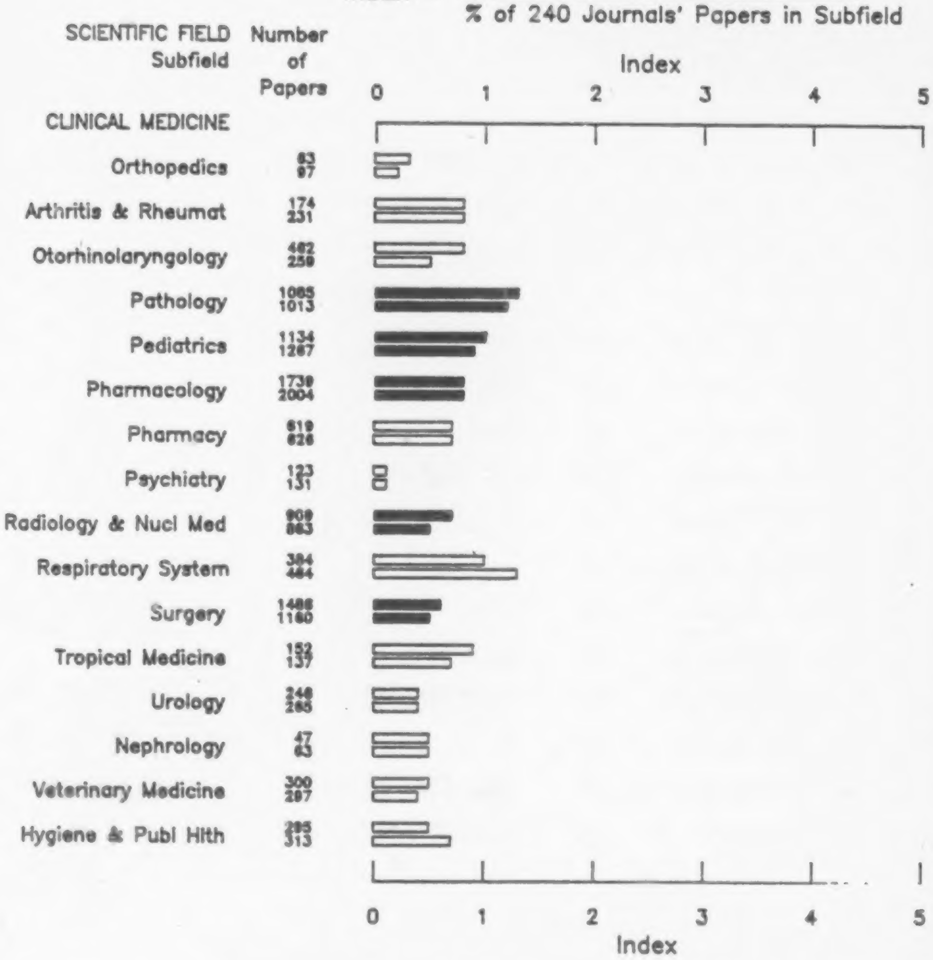
Note: Open bars designate subfields that contained less than 1 percent of the papers acknowledging NIH support in the given period.

Figure 7A (Continued)

Total NIH Activity Indexes in Subfields of Clinical Medicine

240 BID–MEDLINE Journals
1973–1976 over 1977–1980

$$\text{INDEX} = \frac{\%\text{ of Institute's Papers in Subfield}}{\%\text{ of 240 Journals' Papers in Subfield}}$$



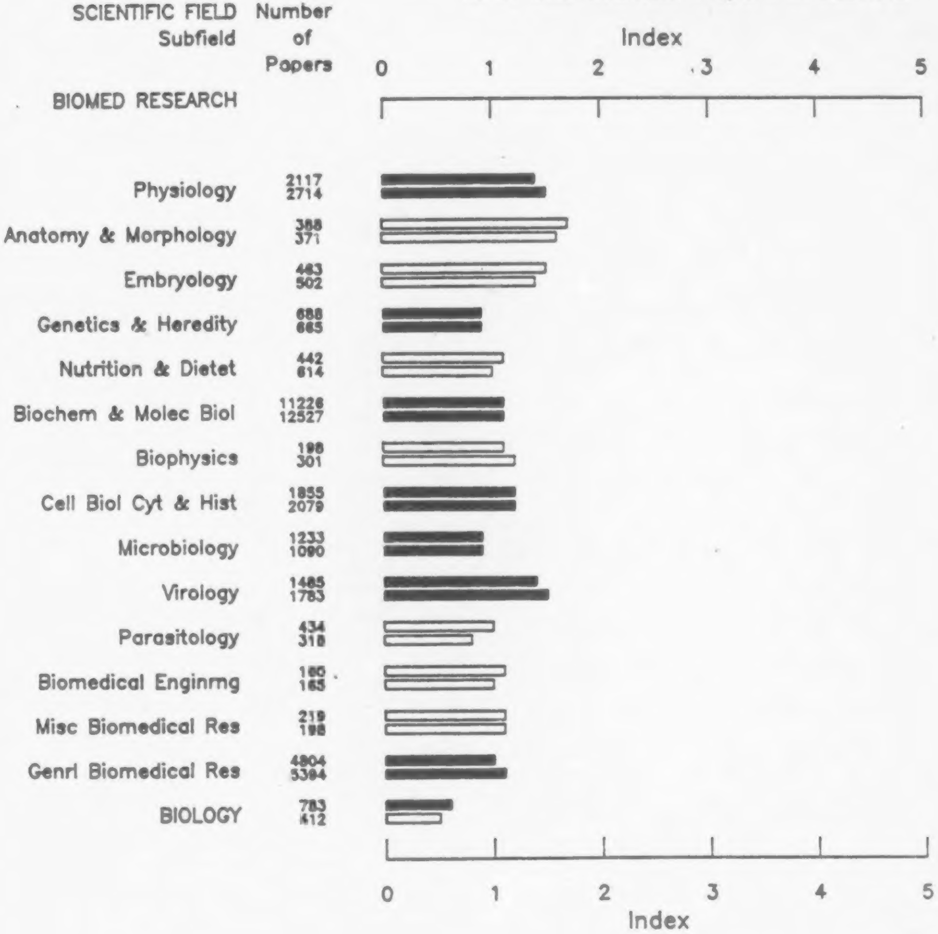
Note: Open bars designate subfields that contained less than 1 percent of the papers acknowledging NIH support in the given period.

Figure 7B

Total NIH Activity Indexes in Subfields of Biomedical Research

240 BID–MEDLINE Journals
1973–1976 over 1977–1980

$$\text{INDEX} = \frac{\text{\% of Institute's Papers in Subfield}}{\text{\% of 240 Journals' Papers in Subfield}}$$



Note: Open bars designate subfields that contained less than 1 percent of the papers acknowledging NIH support in the given period.

Publication Trends -

Another perspective on NIH research dynamics may be gained in comparing the rate of change in NIH-supported papers with changes occurring in Other U.S.- authored and U.S.-supported papers over the same period. Table 4 presents changes for NIH and for Other-U.S. in each of the selected subfields.

Of the total number of papers published by the BIO-MEDLINE journals during 1973-77 and 1977-80, NIH supported 41 and 42 percent. However, the NIH-supported share of papers in basic biomedical journals rose from 50 to 54 percent, while the share of clinical papers decreased from 36 to 34 percent. The Percent Change figures in Table 4 depict these changes by discipline. While the number of NIH-supported biomedical research papers increased 11.7 percent, papers not supported by NIH decreased 7.1 percent. Concurrently, NIH-supported clinical research increased insignificantly (3.4 percent) while clinical research papers not supported by NIH increased 11.7 percent. It is apparent that during the 70's clinical investigators who were not supported by the NIH substantially increased their publication activity. Meanwhile, NIH support shifted slightly toward the more basic biomedical sciences. These results suggest greater independence of clinical research and greater access to alternative sources of support.

Although the overall number of NIH-supported clinical research papers increased only 3.4 percent in the 1977-80 period, that figure masks wide-ranging shifts in emphasis among NIH-supported clinical investigations. These changes range from a 43.9 percent decrease (in Otorhinolaryngology) to a 54 percent increase (in Orthopedics). The NIH role in Otorhinolaryngology declined from 39 to 18 percent as the research papers that were not supported by NIH increased 22.4 percent. The circumstance in Orthopedics is different only with respect to the evidence of increased NIH involvement. The NIH increase is overshadowed by a 78 percent increase in the number of papers supported by other U.S. sources. Despite increased interest, the NIH share of Orthopedics research papers declined from 11 to 9 percent. Other subfields in which the rate of increase in NIH-supported research lagged behind more rapidly increasing activity outside of the NIH purview include Allergy, Arthritis and Rheumatology, Cancer, Nephritis, and Neurology and Neurosurgery.

Other subfields in which NIH support decreased notably, as compared with other U.S., are, (besides Otorhinolaryngology), Anesthesiology, Surgery, General and Internal Medicine, and Dermatology-Venereal Diseases. In all five of these subfields, the number of NIH-supported papers dropped both absolutely and relatively from the 1973-76 period to the 1977-80. In two other fields, Geriatrics and Fertility, both NIH and Other-U.S. papers decreased markedly.

A different kind of dynamic is implied when substantial increases in the number of papers acknowledging NIH support are accompanied by significant decreases in the Other-U.S. category. This kind of change occurred in Hematology, Respiratory System research and Virology. Clearly, strong or rapid increases in programmatic emphases may not immediately change the national pace of production of publishable research. It is conceivable, however, that in the process of drawing a large proportion of the national effort into the NIH milieu, a new vigor may be generated that will later find expression in significant scientific advances and increased productivity. As 1980's data become available, the outcome, if not the operating dynamics, will become evident.

Table 4

Changes in Number and Percent of Papers Supported by NIH and the Rest of the Nation, in Selected Subfields (240 BID-MEDLINE Journals), 1973-76 and 1977-80

	Number of Papers		
	1973-76	1977-80	Percent Change
Fields 1 and 2 Combined			
All NIH	59,945	64,113	7.0
Other U.S.	84,934	89,733	5.7
Clinical Medicine [Field 1]			
All NIH	34,232	35,390	3.4
Other U.S.*	58,994	65,638	11.3
General and Internal Medicine			
All NIH	5,415	4,630	-14.5
Other U.S.	8,551	9,343	9.3
Allergy			
All NIH	147	177	20.4
Other U.S.	155	217	40.0
Anesthesiology			
All NIH	367	242	-34.1
Other U.S.	938	973	3.7
Arthritis and Rheumatism			
All NIH	174	231	32.8
Other U.S.	242	358	47.9
Cancer			
All NIH	3,701	4,257	15.0
Other U.S.	2,274	3,143	38.2
Cardiovascular System			
All NIH	1,911	1,949	2.0
Other U.S.	2,712	2,807	3.5
Dentistry			
All NIH	726	755	4.0
Other U.S.	1,717	1,779	3.6

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*Other U.S. includes all U.S.-authored and U.S.-supported papers except those supported by NIH.

Table 4

Changes in Number and Percent of Papers Supported by NIH
and the Rest of the Nation, in Selected Subfields
(240 BID-MEDLINE Journals), 1973-76 and 1977-80
(Continued)

	Number of Papers		
	1973-76	1977-80	Percent Change
Dermatology and Venereal Diseases			
All NIH	366	329	-10.1
Other U.S.	755	921	22.0
Endocrinology			
All NIH	2,273	2,422	6.6
Other U.S.	1,944	1,590	-18.2
Fertility			
All NIH	298	232	-22.1
Other U.S.	781	636	-18.6
Gastroenterology			
All NIH	466	535	14.8
Other U.S.	782	844	7.9
Geriatrics			
All NIH	162	120	-25.9
Other U.S.	1,046	789	-24.6
Hematology			
All NIH	661	811	22.7
Other U.S.	524	460	-12.2
Immunology			
All NIH	3,457	4,271	23.5
Other U.S.	2,367	2,616	10.5
Nephrology			
All NIH	47	63	34.0
Other U.S.	97	155	59.8
Neurology and Neurosurgery			
All NIH	3,420	3,431	12.0
Other U.S.	3,874	5,147	32.9
Obstetrics and Gynecology			
All NIH	453	516	13.9
Other U.S.	2,049	2,169	5.9

Table 4

Changes in Number and Percent of Papers Supported by NIH and the Rest of the Nation, in Selected Subfields (240 BID-MEDLINE Journals), 1973-76 and 1977-80 (Continued)

	Number of Papers		
	1973-76	1977-80	Percent Change
Ophthalmology			
All NIH	1,194	1,126	-5.7
Other U.S.	1,229	1,467	19.4
Orthopedics			
All NIH	63	97	54.0
Other U.S.	582	1,036	78.0
Otorhinolaryngology			
All NIH	462	259	-43.9
Other U.S.	1,185	1,451	22.4
Pathology			
All NIH	1,085	1,013	-6.6
Other U.S.	1,329	1,459	9.8
Pediatrics			
All NIH	1,134	1,267	11.7
Other U.S.	2,248	2,994	33.2
Pharmacology			
All NIH	1,739	2,004	15.2
Other U.S.	3,256	3,483	7.0
Pharmacy			
All NIH	619	626	1.1
Other U.S.	1,867	1,744	-6.6
Psychiatry			
All NIH	123	131	6.5
Other U.S.	2,483	2,589	4.3
Radio and Nuclear Medicine			
All NIH	909	863	-5.1
Other U.S.	2,845	3,989	40.2
Respiratory System			
All NIH	384	464	20.8
Other U.S.	579	437	-24.5

Table 4

Changes in Number and Percent of Papers Supported by NIH
and the Rest of the Nation, in Selected Subfields
(240 BIO-MEDLINE Journals), 1973-76 and 1977-80
(Continued)

	Number of Papers		
	1973-76	1977-80	Percent Change
Surgery			
All NIH	1,486	1,160	-21.9
Other U.S.	6,127	6,274	2.4
Tropical Medicine			
All NIH	152	137	-9.9
Other U.S.	262	330	26.0
Urology			
All NIH	246	265	7.7
Other U.S.	1,539	1,670	8.5
Veterinary Medicine			
All NIH	300	297	-1.0
Other U.S.	1,583	2,255	42.5
Hygiene and Public Health			
All NIH	295	313	6.1
Other U.S.	1,069	906	-15.2
Biomedical Research [Field 2]			
All NIH	25,711	28,721	11.7
Other U.S.	25,944	24,104	-7.1
Anatomy and Morphology			
All NIH	388	371	-4.4
Other U.S.	250	244	-2.4
Biochemistry and Molecular Biology			
All NIH	11,226	12,527	11.6
Other U.S.	9,119	8,822	-3.3
Biomedical Engineering			
All NIH	160	165	3.1
Other U.S.	242	274	13.2
Biophysics			
All NIH	198	301	52.0
Other U.S.	293	356	21.5

Table 4

Changes in Number and Percent of Papers Supported by NIH and the Rest of the Nation, in Selected Subfields (240 BID-MEDLINE Journals), 1973-76 and 1977-80 (Continued)

	Number of Papers		
	1973-76	1977-80	Percent Change
Embryology			
All NIH	463	502	8.4
Other U.S.	385	421	9.4
Genetics and Heredity			
All NIH	688	665	-3.3
Other U.S.	827	771	-6.8
Microbiology			
All NIH	1,233	1,090	-11.6
Other U.S.	2,009	1,490	-25.8
Nutrition and Dietetics			
All NIH	442	614	38.9
Other U.S.	693	1,027	48.2
Cell Biology, Cytology, and Histology			
All NIH	1,855	2,079	12.1
Other U.S.	1,541	1,572	2.0
Parasitology			
All NIH	434	318	-26.7
Other U.S.	713	627	-12.1
Physiology			
All NIH	2,117	2,714	28.2
Other U.S.	1,723	1,622	-5.9
Virology			
All NIH	1,485	1,783	20.1
Other U.S.	1,099	953	-13.3
General Biomedical Research			
All NIH	4,804	5,394	12.3
Other U.S.	6,697	5,609	-16.2
Miscellaneous Biomedical Research			
All NIH	219	198	-9.6
Other U.S.	351	314	-10.5

NIH CITATION PERFORMANCE

The distribution of the number of citations received by any aggregate of journal papers is extremely skewed. In general, relatively few papers in a field are highly cited, and relatively many are cited once or twice or not at all. Given these skewed distributions, measures of central tendency are of somewhat limited value as analytic tools. By making use of all the information in a distribution of citation rates, however, it is possible to create a statistic that permits comparison of the rates achieved by supported researchers in different disciplines. "T-scores" provide such information (see page 34 for a description of the method of computation). An alternative way of assessing citation impact is to compare the frequency of highly cited papers between groups.

Figure 8* shows the percent of NIH-supported papers that are in the top decile of cited papers in each subfield represented in the BID-MEDLINE journal set. This statistic has the advantage that a top decile is interpretable across both subfields and years, even though the proportions are based upon different numbers of citations in each cited year and in each subfield.

Citations from 1973-80 papers to journal papers published between 1973 and 1977 were used to formulate Figure 8. Graphic representations are limited to the subfields in which more than 1 percent of NIH's supported papers appear.

In each of the 21 subfields in which NIH was most active over the entire period, more than 10 percent of the NIH-supported papers were in the top decile of cited papers. The figure does not reveal that in each of 46 subfields in which NIH supported any papers, more than 10 percent were in the top decile. Moreover, in eight of these subfields, more than 20 percent of the NIH-supported papers were in the top decile (see Table 5).

Historical trends can be observed in Tables 5A and 5B, where complete profiles for the two periods 1973-76 and 1977-80 are presented.

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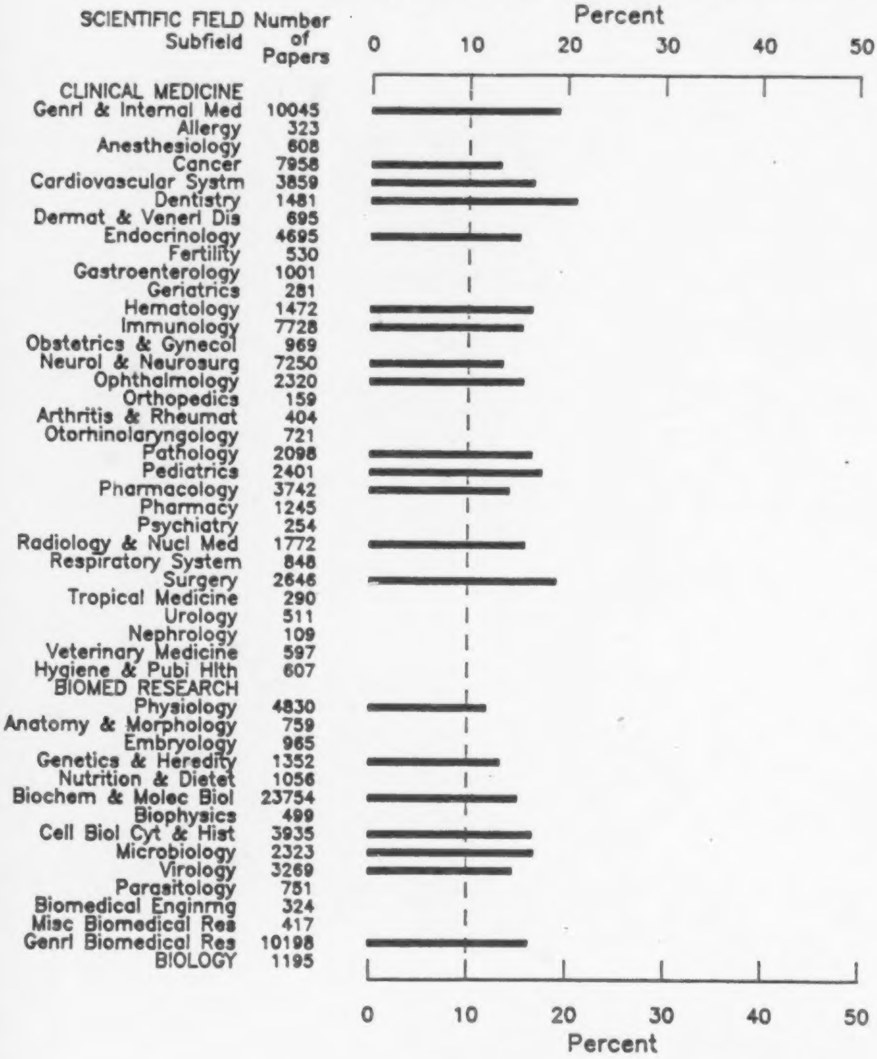
*The data in Figure 8 are not be be compared with those of the corresponding figure in the previous report, which covered the 1970-76 publications (ref.11). Note that the period covered in the present report is 1973-77, and that subfields including fewer than 1 percent of the BID's supported papers are not charted.

Figure 8

Total NIH

Percent of BID's Papers in Top Decile of Cited Papers
1973–1980 Papers in 240 BID–MEDLINE Journals



NOTE: No values shown for scientific subfields with less than 1 percent of papers for this BID.

NIH SUPPORT-SOURCE INTERDEPENDENCY

It is well known that the scientific interests of individual support sources intersect and interact. The lay public and even some scientists have difficulty comprehending the complexity of these relations. Diagrams may be helpful. Figures 9 and 10 are based on mapping the citation interaction among scientists supported by various sources. Corresponding figures in the other reports of this series highlight the role of the individual BIDs.

Figure 9A, based on the references listed in NIH-supported papers, illustrates the dependence of NIH research on information supported by NIH and non-NIH sources. Fifty-two percent of the references in NIH-supported papers were to other papers supported by NIH, and 48 percent were to papers supported by others. The percent of NIH references to each of the BIDs is largely a reflection of their relative sizes. Thus, NCI, NHLBI, NIADDK, and NIGMS receive the largest share of NIH references to NIH-supported papers.

The papers that give no support acknowledgements are likely to cite "clinical observations"--i.e., practicing physicians' observations of notable experience with a small group of patients. Eighteen percent of the NIH references are to papers of foreign (non-U.S.-supported) scientists.

Figure 9B presents the converse of 9A, showing the citations of NIH-supported papers according to the referencing sources. Forty-six percent of the citations received by NIH-supported papers were from papers supported by NIH, while 54 percent were from papers with other support. Again, the percent of NIH citations received from each of the BIDs largely reflects its relative size. NIH receives 23.4 percent of its citations from foreign papers.

Clearly, any decisions that would significantly affect the programmatic structure of NIH would have important effects on a worldwide community of investigators.

Figure 10 represents (a) the various supporters of research reported in the entire journal set, with the areas of the circles proportional to the number of supported papers, and (b) citations by and of NIH-supported papers, showing the same percent distributions as in Figures 9A and 9B. "Foreign," the largest circle, represents papers by authors from foreign institutions who acknowledged no U.S. support. Arrows pointing outward represent references by NIH-supported authors, and arrows pointing inward represent citations of those authors' works.

Figure 9A
PERCENT DISTRIBUTION OF REFERENCES IN NIH-SUPPORTED PAPERS, 1978-80, TO PAPERS SUPPORTED BY NIH AND OTHER SOURCES, 1973-80

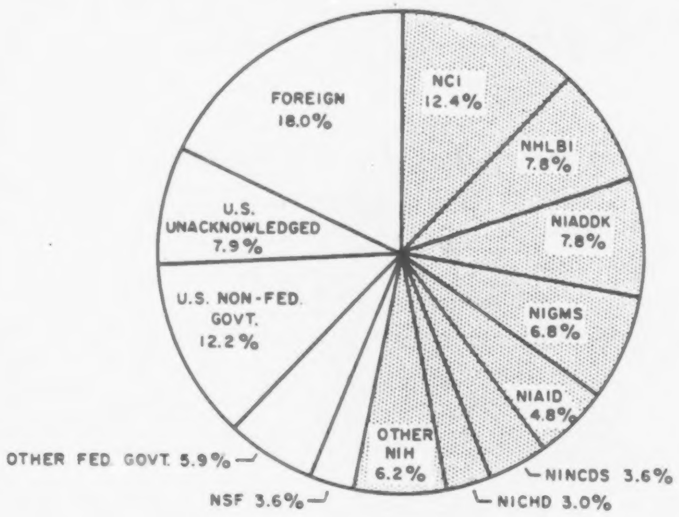


Figure 9B
PERCENT DISTRIBUTION OF CITATIONS OF SUPPORTED PAPERS, 1973-80, IN PAPERS SUPPORTED BY NIH AND OTHER SOURCES, 1978-80

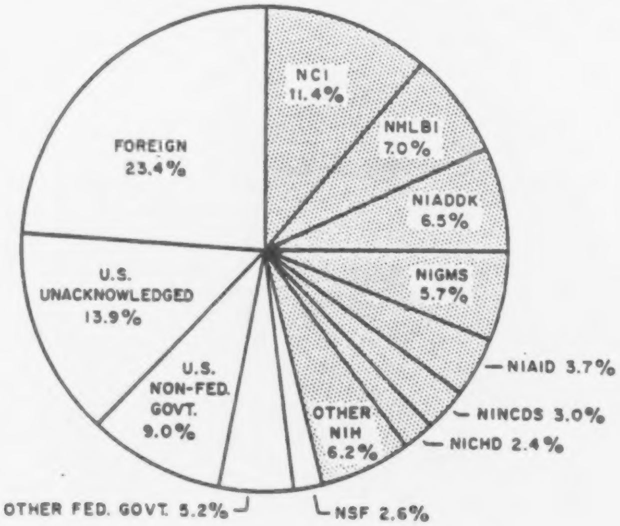
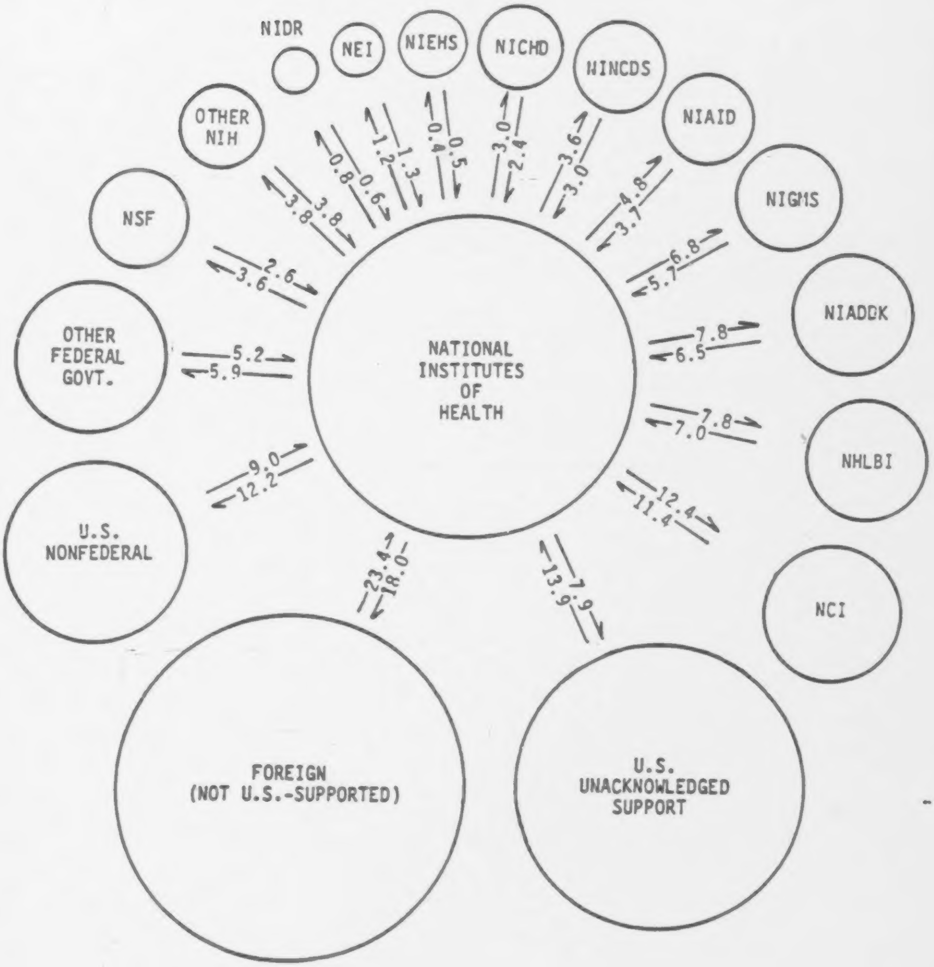


Figure 10

UNIVERSE OF PUBLICATIONS CITED BY AND CITING NIH-SUPPORTED PAPERS

Area of Circles Proportional to Number of Publications Supported; Citations by Percent



NIDR
NEI
NIEHS
NICHD
NINCDS
NIAID
NIGMS
NIADDK
NHLBI
NCI
OTHER NIH
NSF
OTHER FEDERAL GOVT.
U.S. NONFEDERAL
FOREIGN (NOT U.S.-SUPPORTED)
U.S. UNACKNOWLEDGED SUPPORT
NATIONAL INSTITUTES OF HEALTH
3.8
3.8
0.8
0.6
1.2
1.3
0.4
0.5
3.0
2.4
3.6
3.0
4.8
3.7
6.8
5.7
7.8
6.5
7.8
7.0
12.4
11.4
7.9
13.9
23.4
18.0
9.0
12.2
5.2
5.9
2.6
3.6

PUBLICATION PROFILE*

Table 5A is a profile of the bibliometric activity of NIH for the period 1973-76. It counts all papers published in the 240 BID-MEDLINE journal set in the years 1973-76 and counts citations received by these papers from the 275-journal set from 1973 through 1980.

Similarly, Table 5B is a profile of NIH for the period 1977-80.

The first page of each table presents the data for all fields combined, for each research level, and for each of the major fields. The second page lists the individual subfields of clinical medicine and biomedical research. The column headings are defined as follows:

1 Number of Papers - The fractional number of papers supported by NIH in the particular level, field, and subfield (L/F/S).

2 Activity Index - Proportion of NIH's papers in the L/F/S divided by the proportion of all papers in the BID-MEDLINE journal set in that L/F/S.

3 % Internal Effort -- Percent of NIH's papers in the particular L/F/S.

4 % External Effort - Percent of all papers in the BID-MEDLINE journal set in the particular L/F/S that were supported by NIH.

5 Total Cites - Total citations (from all journals in the BID-MEDLINE set for citing years 1973-80) received by the papers supported by NIH in the particular L/F/S. Scaled to the average citation rate for each L/F/S in 1973.

6 Cites per Paper - Total scaled citations received by NIH's papers in a given L/F/S, divided by the number of papers supported.

7 Cite T-Score - NIH's average citations per paper minus the average citations per paper for all papers in the particular L/F/S, divided by the standard deviation of citations per paper for all papers in that L/F/S. The statistic is scaled to a mean of 50 and a standard deviation of 10.

8 % Papers Among the Top 10% - Percent of NIH's papers in the particular L/F/S that are among the 10 percent most highly cited papers in that L/F/S.

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*Although the publication profile presents analyses for any number of papers, the data are likely to be unstable when based on aggregates of less than 25. The skewness of citation distributions permits only approximate statements about confidence limits. It may be said, however, that a sample size of 20 is required to achieve a 95 percent confidence interval of ±2 citations.

Table 5A

BIBLIOMETRIC PROFILE OF NIH-
SUPPORTED RESEARCH, 1973-76*

FIELD/LEVEL	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
************************ NORMALIZED AGAINST FIELDS [1-2] ************************								
FIELDS [1-2]	59945.	1.00	100.00	29.11	852029.	14.2	53.15	16.28
CLIN MEDICINE [1]	34232.	0.95	57.11	27.61	395714.	11.6	54.69	17.92
BIOMED RESEARCH [2]	25711.	1.08	42.89	31.38	457077.	17.8	52.30	15.50
LEVEL								
CLINICAL-MIX [1-2]	14377.	0.72	23.98	21.07	137827.	9.6	55.67	19.53
CLIN INVESTIGATN [3]	18250.	1.25	30.44	36.35	227478.	12.5	53.64	15.33
BASIC RESEARCH [4]	27316.	1.07	45.57	31.22	487059.	17.8	52.27	15.08
************************ NORMALIZED AGAINST FIELDS [1-9] ************************								
FIELDS [1-9]	62421.	1.00	100.00	28.16	865353.	13.9	53.32	16.92
CLIN MEDICINE [1]	34232.	0.98	54.84	27.61	395714.	11.6	54.69	17.92
BIOMED RESEARCH [2]	25711.	1.11	41.19	31.38	457077.	17.8	52.30	15.50
BIOLOGY [3]	783.	0.60	1.25	16.83	3829.	4.9	52.24	15.76
CHEMISTRY [4]	827.	0.80	1.32	22.59	7879.	9.5	53.36	15.12
PHYSICS [5]	119.	0.97	0.19	27.28	865.	7.3	55.27	20.65
EARTH & SPACE SC [6]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
ENGRNG & TECHNOL [7]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
PSYCHOLOGY [8]	748.	0.38	1.20	10.67	3314.	4.4	54.91	21.14
MATHEMATICS [9]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00

NOTE: CHEMISTRY AND PSYCHOLOGY DATA SHOULD BE TREATED CAUTIOUSLY OVER TIME DUE TO INCONSISTENT DATABASE COVERAGE.

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*BID-SCI journal set citing BID-MEDLINE papers, 1973-80. Activity index normalized against Fields 1 and 2. Citation counts scaled within subfield to 1973 equivalents.

Table 5A (Continued)

BIBLIOMETRIC PROFILE OF NIH-
SUPPORTED RESEARCH, 1973-76*

FIELD/SUBFIELD	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
CLIN MEDICINE [1]								
GENRL & INTERNAL MED	5415.	1.00	9.03	29.10	84240.	15.6	56.18	18.50
ALLERGY	147.	1.45	0.24	42.10	1157.	7.9	51.24	13.08
ANESTHESIOLOGY	367.	0.88	0.61	25.61	2301.	6.3	56.09	22.82
CANCER	3701.	1.68	6.17	49.00	51296.	13.9	52.29	13.33
CARDIOVASCULAR SYSTM	1911.	1.19	3.19	34.68	29803.	15.6	55.34	16.30
DENTISTRY	726.	0.71	1.21	20.74	3225.	4.4	54.91	21.16
DERMAT & VENERL DIS	366.	0.95	0.61	27.74	1905.	5.2	56.42	19.78
ENDOCRINOLOGY	2273.	1.24	3.79	36.06	33639.	14.8	55.23	14.75
FERTILITY	298.	0.54	0.50	15.64	1590.	5.3	51.48	14.92
GASTROENTEROLOGY	466.	0.98	0.78	28.54	4971.	10.7	56.96	16.31
GERIATRICS	162.	0.40	0.27	11.77	557.	3.4	56.97	28.84
HEMATOLOGY	661.	1.01	1.10	29.26	5702.	8.6	53.77	16.15
IMMUNOLOGY	3457.	1.43	5.77	41.77	59210.	17.1	53.64	15.77
OBSTETRICS & GYNECOL	453.	0.50	0.76	14.49	3549.	7.8	54.41	17.48
NEUROL & NEUROSURG	3420.	0.98	5.70	28.65	41968.	12.3	51.98	13.30
OPHTHALMOLOGY	1194.	1.44	1.99	62.02	6985.	5.9	52.98	15.62
ORTHOPEDICS	63.	0.27	0.10	7.79	392.	6.3	56.98	22.13
ARTHRITIS & RHEUMAT	174.	0.81	0.29	23.62	1990.	11.4	62.43	21.86
OTORHINOLARYNGOLOGY	462.	0.82	0.77	23.74	1636.	3.5	53.35	16.52
PATHOLOGY	1085.	1.29	1.81	37.41	8411.	7.8	53.63	15.61
PEDIATRICS	1134.	0.95	1.89	27.71	8282.	7.3	54.92	16.23
PHARMACOLOGY	1739.	0.78	2.90	22.64	19470.	11.2	52.53	15.42
PHARMACY	619.	0.70	1.03	20.38	4052.	6.5	54.16	18.31
PSYCHIATRY	123.	0.13	0.21	3.73	794.	6.4	53.67	15.97
RADIOLOGY & NUCL MED	909.	0.72	1.52	20.82	5324.	5.9	52.20	14.67
RESPIRATORY SYSTEM	384.	1.01	0.64	29.37	3177.	8.3	52.99	16.31
SURGERY	1486.	0.57	2.48	16.49	10662.	7.2	54.74	18.54
TROPICAL MEDICINE	152.	0.94	0.25	27.37	635.	4.2	51.78	14.79
UROLOGY	246.	0.40	0.41	11.55	1090.	4.4	53.38	18.55
NEPHROLOGY	47.	0.55	0.08	15.98	249.	5.4	51.85	10.04
VETERINARY MEDICINE	300.	0.52	0.50	15.02	922.	3.1	51.42	15.37
ADDICTIVE DISEASES	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
HYGIENE & PUBL HLTH	295.	0.53	0.49	15.47	1787.	6.1	61.01	27.77
BIOMED RESEARCH [2]								
PHYSIOLOGY	2117.	1.36	3.53	39.53	31284.	14.8	51.02	11.76
ANATOMY & MORPHOLOGY	388.	1.65	0.65	48.14	2360.	6.1	51.05	13.23
EMBRYOLOGY	463.	1.45	0.77	42.34	5666.	12.2	53.55	14.54
GENETICS & HEREDITY	688.	0.91	1.15	26.55	6829.	9.9	50.58	11.78
NUTRITION & DIETET	442.	1.06	0.74	30.81	3608.	8.2	55.52	15.81
BIOCHEM & MOLEC BIOL	11226.	1.07	18.73	31.06	214266.	19.1	51.83	15.02
BIOPHYSICS	198.	1.12	0.33	32.62	1738.	8.8	55.40	17.26
CELL BIOL CYT & HIST	1855.	1.17	3.10	34.15	32892.	17.7	53.19	16.41
MICROBIOLOGY	1233.	0.86	2.06	25.13	12345.	10.0	54.34	17.39
VIROLOGY	1485.	1.40	2.48	40.74	30308.	20.4	54.17	14.80
PARASITOLOGY	434.	1.01	0.72	29.37	1694.	3.9	53.25	17.88
BIOMEDICAL ENGINRNG	160.	1.09	0.27	31.68	490.	3.1	55.11	17.33
MISC BIOMEDICAL RES	219.	1.09	0.37	31.71	457.	2.1	51.79	15.69
GENRL BIOMEDICAL RES	4804.	0.96	8.01	27.82	115314.	24.0	54.22	16.98

Table 5B

BIBLIOMETRIC PROFILE OF NIH-
SUPPORTED RESEARCH, 1977-80*

FIELD/LEVEL		NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
************************ NORMALIZED AGAINST FIELDS [1-2] ************************									
FIELDS [1-2]		64113.	1.00	100.00	27.95	447666.	14.1	54.21	17.37
CLIN MEDICINE	[1]	35390.	0.90	55.20	25.22	208123.	11.8	55.68	19.62
BIOMED RESEARCH	[2]	28721.	1.15	44.80	32.25	237624.	17.0	53.05	14.88
LEVEL									
CLINICAL-MIX	[1-2]	13626.	0.63	21.25	17.69	70005.	9.9	55.86	22.05
CLIN INVESTIGATN	[3]	19601.	1.23	30.57	34.51	120121.	12.5	54.78	15.79
BASIC RESEARCH	[4]	30882.	1.16	48.17	32.30	254503.	16.9	52.95	14.63
************************ NORMALIZED AGAINST FIELDS [1-9] ************************									
FIELDS [1-9]		65688.	1.00	100.00	27.45	445791.	13.7	54.31	18.03
CLIN MEDICINE	[1]	35390.	0.92	53.88	25.22	208123.	11.8	55.68	19.62
BIOMED RESEARCH	[2]	28721.	1.17	43.72	32.25	237624.	17.0	53.05	14.88
BIOLOGY	[3]	412.	0.48	0.63	13.20	1257.	5.1	52.99	20.96
CHEMISTRY	[4]	463.	0.60	0.70	16.58	3114.	10.1	54.05	17.43
PHYSICS	[5]	162.	1.41	0.25	38.84	465.	5.9	52.44	14.59
EARTH & SPACE SC	[6]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
ENGRNG & TECHNOL	[7]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
PSYCHOLOGY	[8]	538.	0.55	0.82	15.08	1184.	4.3	54.40	22.18
MATHEMATICS	[9]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00

NOTE: CHEMISTRY AND PSYCHOLOGY DATA SHOULD BE TREATED CAUTIOUSLY OVER TIME DUE TO INCONSISTENT DATABASE COVERAGE.

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*BID-SCI journal set citing BID-MEDLINE papers, 1973-80, but does not include citations received by 1979-80 publications. Activity index normalized against Fields 1 and 2. Citation counts scaled within subfield to 1973 equivalents.

Table 5B (Continued)

BIBLIOMETRIC PROFILE OF NIH-
SUPPORTED RESEARCH, 1977-80*

FIELD/SUBFIELD	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
CLIN MEDICINE [1]								
GENRL & INTERNAL MED	4630.	0.86	7.22	24.13	41909.	17.2	57.24	20.31
ALLERGY	177.	1.34	0.28	37.59	720.	8.7	53.55	16.16
ANESTHESIOLOGY	242.	0.64	0.38	17.88	784.	7.1	59.00	25.68
CANCER	4257.	1.59	6.64	44.31	30045.	13.6	52.55	13.07
CARDIOVASCULAR SYSTM	1949.	1.18	3.04	33.04	14874.	15.3	56.08	17.07
DENTISTRY	755.	0.74	1.18	20.75	1612.	4.1	53.11	20.37
DERMAT & VENERL DIS	329.	0.73	0.51	20.40	859.	5.8	55.74	28.49
ENDOCRINOLOGY	2422.	1.29	3.78	36.17	16254.	15.3	58.25	16.18
FERTILITY	232.	0.45	0.36	12.65	654.	5.5	51.51	18.04
GASTROENTEROLOGY	535.	0.96	0.83	26.75	3054.	10.5	63.99	16.35
GERIATRICS	120.	0.38	0.19	10.69	231.	4.5	62.42	26.69
HEMATOLOGY	811.	1.12	1.27	31.29	3048.	8.8	63.15	17.26
IMMUNOLOGY	4271.	1.45	6.66	40.50	34324.	16.1	56.09	14.97
OBSTETRICS & GYNECOL	516.	0.54	0.81	15.19	2147.	8.3	55.32	22.84
NEUROL & NEUROSURG	3831.	0.95	5.97	26.51	23506.	12.2	53.21	13.77
OPHTHALMOLOGY	1126.	1.32	1.76	36.91	3147.	6.1	52.94	15.66
ORTHOPEDICS	97.	0.23	0.15	6.33	174.	5.4	53.35	18.56
ARTHRITIS & RHEUMAT	231.	0.79	0.36	22.14	906.	10.5	54.63	22.93
OTORHINOLARYNGOLOGY	259.	0.47	0.40	13.00	655.	4.2	54.14	18.57
PATHOLOGY	1013.	1.21	1.58	33.69	4001.	8.2	56.55	18.63
PEDIATRICS	1267.	0.86	1.98	24.00	4772.	7.7	55.21	19.89
PHARMACOLOGY	2004.	0.77	3.12	21.55	9003.	9.8	51.11	11.80
PHARMACY	626.	0.72	0.98	20.06	2389.	6.8	54.94	20.27
PSYCHIATRY	131.	0.14	0.20	3.79	582.	8.1	58.15	22.17
RADIOLOGY & NUCL MED	863.	0.54	1.35	15.15	2805.	5.9	51.91	18.00
RESPIRATORY SYSTEM	464.	1.28	0.72	35.71	1882.	8.2	61.36	18.60
SURGERY	1160.	0.45	1.81	12.58	4744.	7.3	54.31	20.21
TROPICAL MEDICINE	137.	0.70	0.21	19.54	361.	4.9	53.61	14.67
UROLOGY	265.	0.39	0.41	10.90	764.	5.2	55.26	21.96
NEPHROLOGY	63.	0.50	0.10	14.11	131.	3.6	48.94	14.93
VETERINARY MEDICINE	297.	0.38	0.46	10.59	505.	3.4	52.57	15.62
ADDICTIVE DISEASES	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
HYGIENE & PUBL HLTH	313.	0.71	0.49	19.92	933.	6.0	60.41	38.63
BIOMED RESEARCH [2]								
PHYSIOLOGY	2714.	1.51	4.23	42.18	18683.	14.7	51.36	12.08
ANATOMY & MORPHOLOGY	371.	1.64	0.58	45.97	1234.	6.2	51.84	17.75
EMBRYOLOGY	502.	1.35	0.78	37.85	2849.	11.5	55.90	15.20
GENETICS & HEREDITY	665.	0.86	1.04	24.04	3099.	9.9	52.45	16.56
NUTRITION & DIETET	614.	0.97	0.96	27.24	2400.	7.7	52.62	14.78
BIOCHEM & MOLEC BIOL	12527.	1.11	19.54	30.93	111233.	18.6	53.40	15.18
BIOPHYSICS	301.	1.20	0.47	33.67	997.	8.1	52.53	13.18
CELL BIOL CYT & HIST	2679.	1.25	3.24	34.82	17959.	17.5	56.39	16.93
MICROBIOLOGY	1090.	0.90	1.70	25.17	4565.	8.8	53.50	15.30
VIROLOGY	1783.	1.52	2.78	42.37	16735.	19.3	61.04	14.33
PARASITOLOGY	318.	0.82	0.50	23.03	734.	3.7	52.23	14.06
BIOMEDICAL ENGINRNG	165.	0.98	0.26	27.35	285.	3.2	55.72	29.26
MISC BIOMEDICAL RES	198.	1.14	0.31	31.98	243.	2.2	51.96	16.57
GENRL BIOMEDICAL RES	5394.	1.14	8.41	31.78	57521.	21.2	53.70	14.73

CROSSCUTTING RESEARCH

Table 6 opens a small window on the breadth of relations between biomedical disciplines and the programmatic interests of NIH. Shown in the table are the clinical medical fields and basic bioscience disciplines that were substantially supported by more than one NIH Institute, as reflected in 1973-76 and 1977-80 publications. Seventy-five papers in either time period is the arbitrary minimum number of papers used here to define substantial involvement. Publication counts for each discipline and BID show changes of research emphasis over time.

For the following 15 other disciplines, only one BID each was substantially involved. The Institute and number of papers in each period, 1973-76/1977-80, are shown parenthetically.

Allergy (NIAID--98/106 papers)
Anesthesiology (NIGMS--230/143 papers)
Cardiovascular System (NHLBI--1,626/1,661 papers)
Dentistry (NIDR--554/574 papers)
Fertility (NICHD--198/160 papers)
Gastroenterology (NIADDK--298/347 papers)
*Geriatrics (NICHD + NIA--71 + 17/13 + 67 papers)
Ophthalmology (NEI--995/994 papers)
Arthritis and Rheumatism (NIADDK--109/127 papers)
Otorhinolaryngology (NINCDS--345/159 papers)
Respiratory System (NHLBI--253/347 papers)
Tropical Medicine (NIAID--120/108 papers)
Hygiene and Public Health (NHLBI--49/81 papers)
Anatomy and Morphology (NICHD--88/83 papers)
Parasitology (NIAID--352/231 papers)

The fields and disciplines that have been most widely influenced by NIH programmatic interests--i.e., four or more of the Institutes supported a substantial number of papers--are as follows:

General and Internal Medicine
Cancer
Endocrinology
Immunology
Neurology and Neurosurgery
Pathology
Pediatrics
Pharmacology
Surgery
Physiology
Biochemistry and Molecular Biology
Cell Biology, Cytology, and Histology
Microbiology

Not surprisingly, all the BIDs supported a substantial number of papers in the subfield Biochemistry and Molecular Biology.

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*Following the creation of NIA in 1974, most of the Geriatrics research formerly sponsored by NICHD was subsequently transferred to the new Institute. Hence, publication counts in this subfield for NIA and NICHD are presented together here.

Table 6

CROSSCUTTING BIOMEDICAL SUBFIELDS
Number of BID-Supported Papers During 1973-76 and 1977-80*

Subfields	NCI	NEI	NHLBI	NIAID	NIADDK	NICHD	NIDR	NIGMS	NINCDS	NIA**	NIEHS
Gen. & Int. Medicine	707 688	-	1253 1184	570 404	1264 1068	311 221	-	372 254	138 110	-	-
Cancer	3062 3680	-	-	85 63	81 79	-	-	104 84	-	-	-
Dermat. & VD	81 61	-	-	-	186 144	-	-	-	-	-	-
Endocrinology	135 179	-	128 173	-	890 928	605 622	-	-	79 65	-	-
Hematology	136 262	-	234 285	-	134 102	-	-	-	-	-	-
Immunology	811 1344	-	151 220	1563 1685	343 325	72 91	75 58	163 159	44 77	-	-
Obstetrics & Gynecology	67 81	-	-	-	-	191 206	-	-	-	-	-
Neurology & Neurosurgery	-	373 548	66 84	-	56 82	226 241	-	206 201	2078 2178	-	-
Pathology	189 227	-	258 277	-	173 158	-	-	79 42	-	-	-
Pediatrics	78 96	-	115 227	100 97	155 159	302 315	-	59 74	-	-	-
Pharmacology	204 263	-	311 398	-	165 175	80 77	-	373 377	253 250	-	168 235
Pharmacy	224 262	-	-	-	-	-	-	119 133	-	-	-

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*Counts shown only if two or more BIDs had at least 75 papers each in the subfield in either period.

**NIA was created in 1974 and had few papers during 1973-76.

Table 6

CROSSCUTTING BIOMEDICAL SUBFIELDS (continued)
Number of BID-Supported Papers During 1973-76 and 1977-80*

Subfields	NCI	NEI	NHLBI	NIAID	NIADDK	NICHD	NIDR	NIGMS	NINCDS	NIA**	NIEHS
Radiology & Nucl. Medicine	315 364	-	153 181	-	-	-	-	222 153	-	-	-
Surgery	179 146	-	502 397	-	315 235	-	-	205 174	-	-	-
Urology	66 100	-	-	-	80 178	-	-	-	-	-	-
Physiology	-	81 119	853 1219	-	196 568	85 121	-	158 155	328 265	-	-
Embryology	-	-	-	-	-	179 162	-	86 99	-	-	-
Genetics & Heredity	81 137	-	-	-	-	-	-	330 288	-	-	-
Nutrition & Diet	-	-	-	-	180 227	63 84	-	-	-	-	-
Biochem. & Molec. Biol.	1733 2136	97 136	1349 1836	602 532	2506 2458	716 649	135 146	2731 3136	519 430	13 95	82 129
Cell Biol. Cyto. & Hist.	485 605	-	133 170	81 60	227 305	184 127	86 64	353 370	145 138	-	-
Microbiology	95 90	-	-	399 289	105 62	-	-	447 488	-	-	-
Virology	683 1047	-	-	458 419	-	-	-	180 180	-	-	-

PART II. NIH INTRAMURAL PROGRAM

Part I of this report presented a bibliometric analysis of all NIH-supported publications--intramural and extramural. This section focuses on the publications resulting from the NIH Intramural Research Program.

This program yields approximately 10 percent of all NIH-supported publications, varying across the individual BIDs. Funding for these programs as a percent of the BID's total budget ranges from less than 1 for NIGMS to nearly 30 for NIEHS. Table 7 presents obligations data for the individual Institutes.

The other tables and figures in this part of the report parallel those in Part I.

Table 7

Allocation of Individual BIDs' Fiscal 1980 Obligations
to the Intramural Research Program*
(Dollars in Thousands)

BID	Total Obligations	Intramural Research	Percent
NIA	$ 69,687	$ 12,670	18.2%
NIAID	214,657	37,108	17.3
NIADDK	340,131	40,387	11.9
NCI	998,047	144,009	14.4
NICHD	208,346	21,593	10.4
NIDR	67,600	13,039	19.3
NIEHS	83,637	24,897	29.8
NEI	109,603	10,192	9.3
NIGMS	312,339	515	0.2
NHLBI	527,091	39,040	7.4
NINCDS	241,353	34,473	14.3

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*Data from "Basic Data Relating to the National Institutes of Health, 1981," NIH Publication No. 81-1261, May 1981, pp. 12-17.

INTRAMURAL FUNDING AND PUBLICATION TRENDS

As in the NIH overall program, analysis of intramural data reveals a strong association of funding and publication trends. The correlation between intramural research obligations in constant (fiscal 1969) dollars, 1967-77, and numbers of research papers published three years later (Fields 1-9) proved substantial: r = .93. The two series are as follows:

Fiscal Year	Constant $ (Thousands)	Fiscal Year	No. of Papers
1967	$ 95,231	1970	1,285
1968	100,425	1971	1,326
1969	104,473	1972	1,417
1970	102,640	1973	1,348
1971	116,250	1974	1,379
1972	118,408	1975	1,427
1973	120,518	1976	1,462
1974	127,417	1977	1,542
1975	137,786	1978	1,598
1976	143,320	1979	1,766
1977	160,089	1980	1,672*

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*Approximately 5 percent short of total papers.

INTRAMURAL PUBLICATION ACTIVITY

A research-level profile of papers derived from the NIH Intramural Research Program (IRP) is presented in Table 8, and publication profiles showing the areas of NIH IRP research emphasis are presented in Figures 11A, 11B, 12A, and 12B. These figures are constructed directly from the data in Tables 9A and B.

Research-Level Profile

Table 8 presents the level classification of the NIH IRP publications for two time periods, 1973-76 and 1977-80. There was a decrease in the percent, but not the number, of IRP papers at the more clinical levels (Levels 1 and 2) and an increase in the number and percent of IRP papers at the more basic levels--Clinical Investigation (Level 3) and Basic Research (Level 4). These trends closely parallel those noted in the total NIH supported papers (intramural and extramural) in Table 3.

Table 8

Number and Percent of NIH Intramural Research Papers According to Level, 1973-76 and 1977-80

Level	1973-76		1977-80*	
Levels 1 & 2 (Clinical Observation & Clinical Mix)	1,209	22%	1,273	19%
Level 3 (Clinical Investigation)	1,887	34	2,300	35
Level 4 (Basic Research)	2,425	44	3,020	46
Total	5,521	100%	6,593	100%

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*1980 data include a 5 percent estimate for 1980 papers appearing on 1981 SCI tapes.

Publication Counts

Figures 11A and 11B show the percent of all papers in clinical medicine and biomedical research, respectively, in the BIO-MEDLINE journal set that were supported by NIH. For each subfield, the two sets of bars represent NIH-supported papers as a percent of all papers in the subfield, 1973-76 and 1977-80. All papers acknowledging NIH support, intramural or extramural, are indicated by the total bar; those acknowledging IRP support, by the dark portion.

The areas in which NIH plays the largest role--i.e., greatest relative emphasis--are Cancer, Immunology, and Virology. This emphasis reflects the large roles of the National Cancer Institute and the National Institute of Allergy and Infectious Diseases, the first in all three areas and the second in Immunology and Virology. The IRP as well as NIH altogether is a major force in these three subfields.

Activity Indexes

Figures 12A and 12B show the activity index distribution for the IRP at the two periods 1973-76 and 1977-80. A fuller description of the activity index is provided on page 16.

The IRP activity index in Cancer, at 3.3 for 1973-76 and 2.8 for 1977-80 (or 3.3 and 2.8 times the "expected" level, given the size of the IRP and the size of the field), is the program's subfield of greatest relative emphasis. Note that the index for Cancer declined in the second period, though the number of IRP papers in the subfield actually increased. This is because the subfield grew faster than the IRP participation.

The IRP's activity indexes are high in the subfields of Immunology and Virology. During 1977-80 the IRP increased its absolute and relative activity in these areas.

The indexes are also high for certain subfields, represented by open bars, that contained very few of the papers acknowledging IRP support, such as Tropical Medicine, Embryology, and Miscellaneous Biomedical Research. While NIH does not emphasize these subfields, the research is important to sustain and advance areas not attractive to many investigators.

Figure 11A

NIH Intramural and Total NIH

Percent of All Papers in Each Subfield of Clinical Medicine

240 BID–MEDLINE Journals

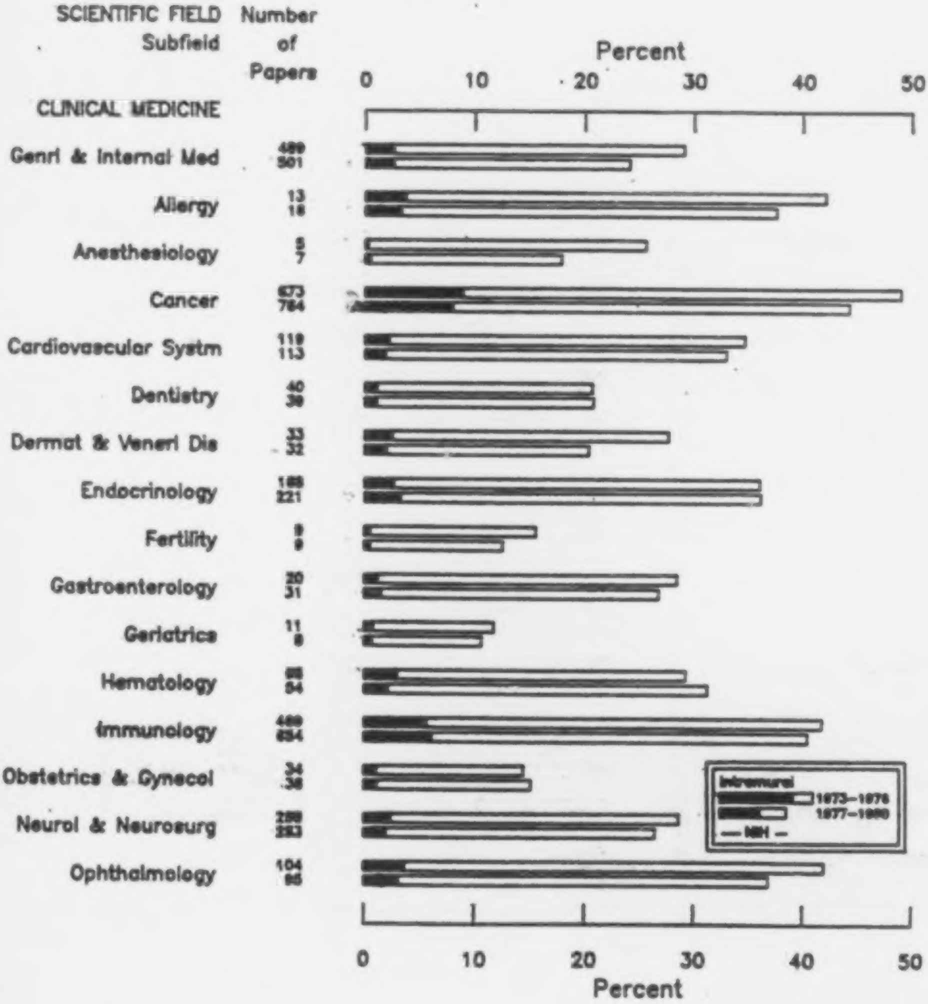
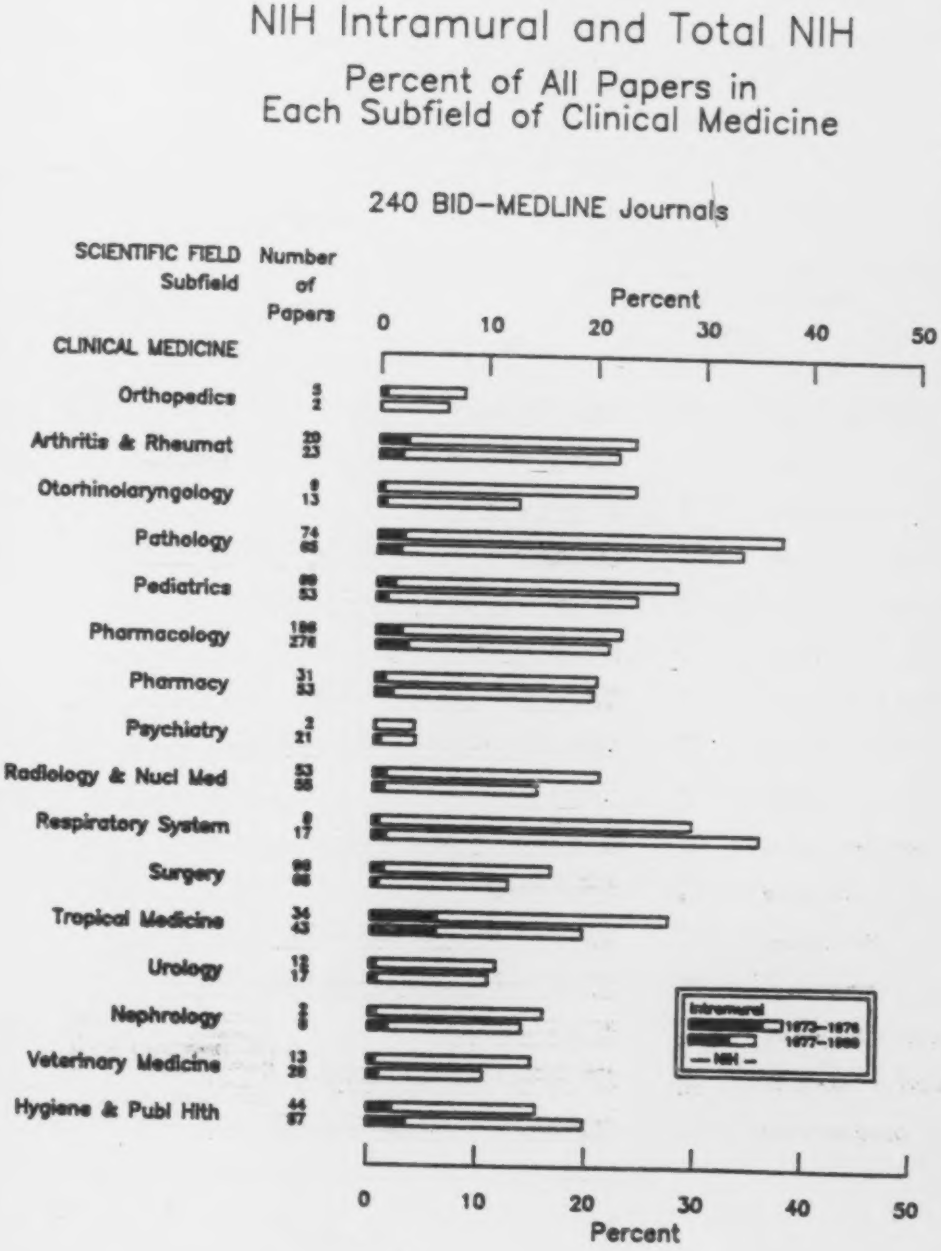


Figure 11A (Continued)



NIH Intramural and Total NIH

Percent of All Papers in Each Subfield of Clinical Medicine

240 BID–MEDLINE Journals

Figure 11B

NIH Intramural and Total NIH

Percent of All Papers in Each Subfield of Biomedical Research

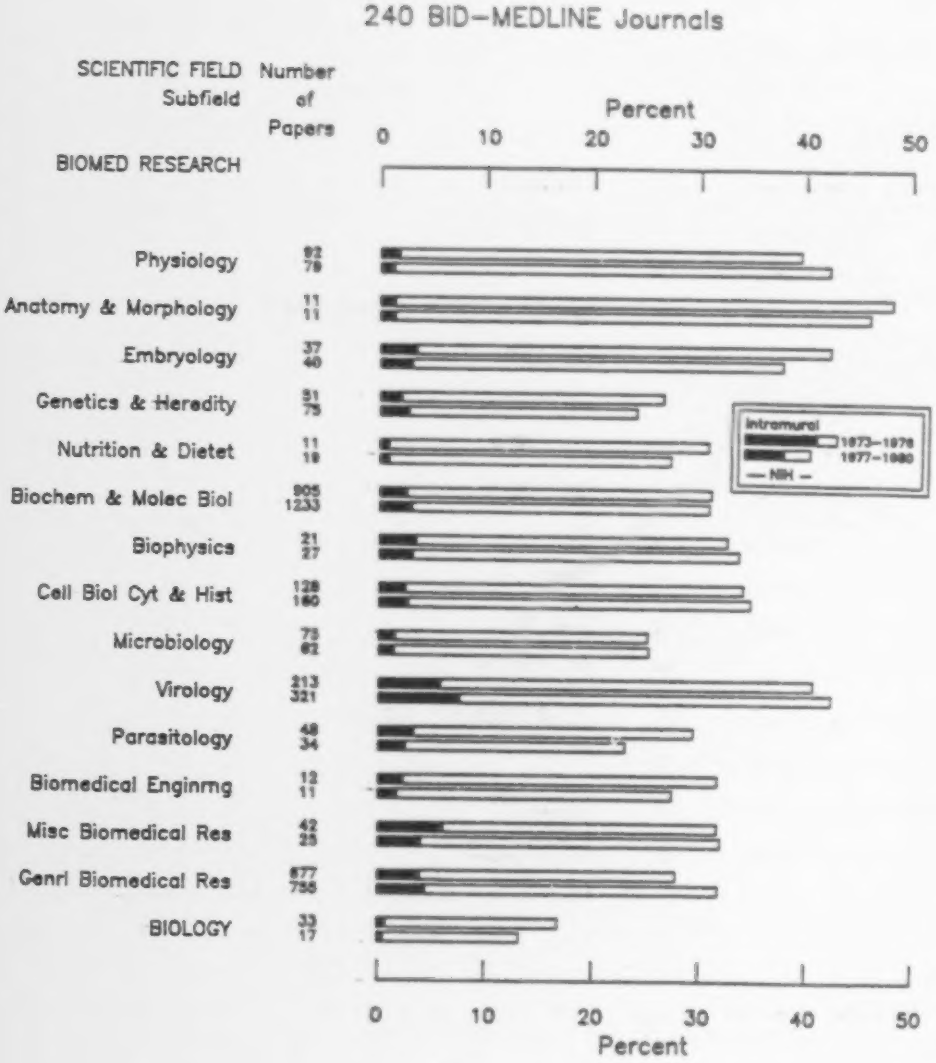
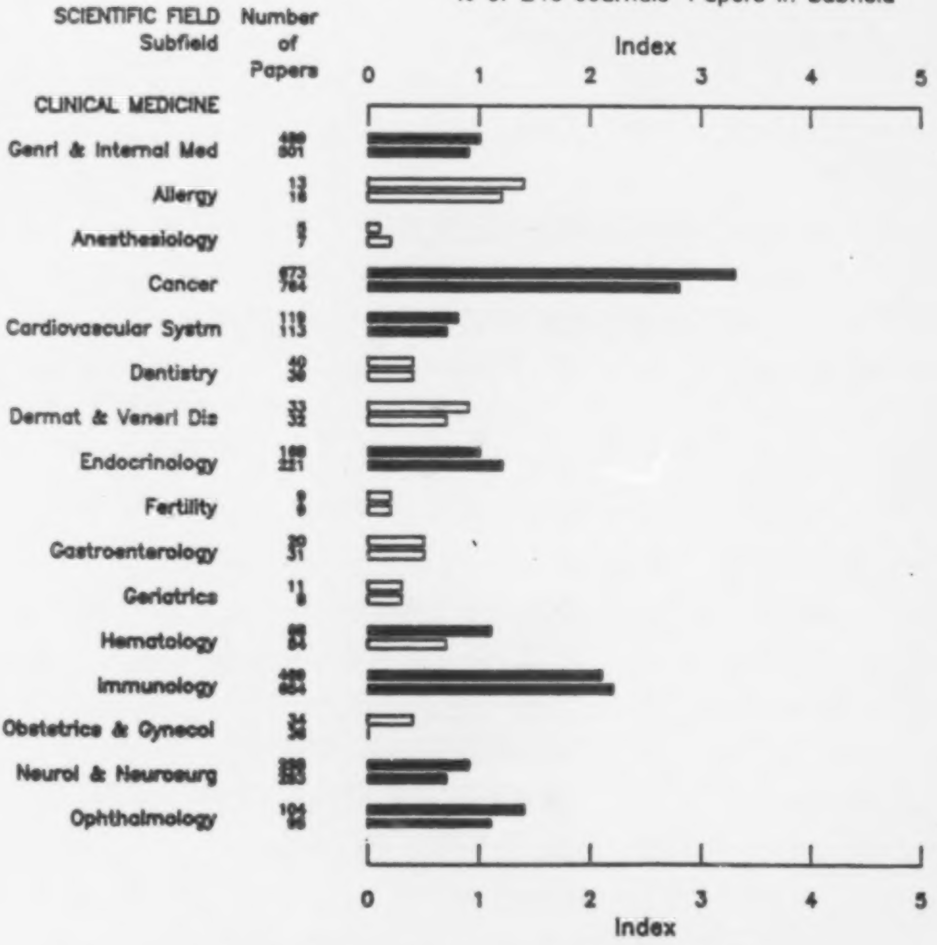


Figure 12A

NIH Intramural Activity Indexes in Subfields of Clinical Medicine

240 BID—MEDLINE Journals
1973—1976 over 1977—1980

$$\text{INDEX} = \frac{\text{\% of Institute's Papers in Subfield}}{\text{\% of 240 Journals' Papers in Subfield}}$$



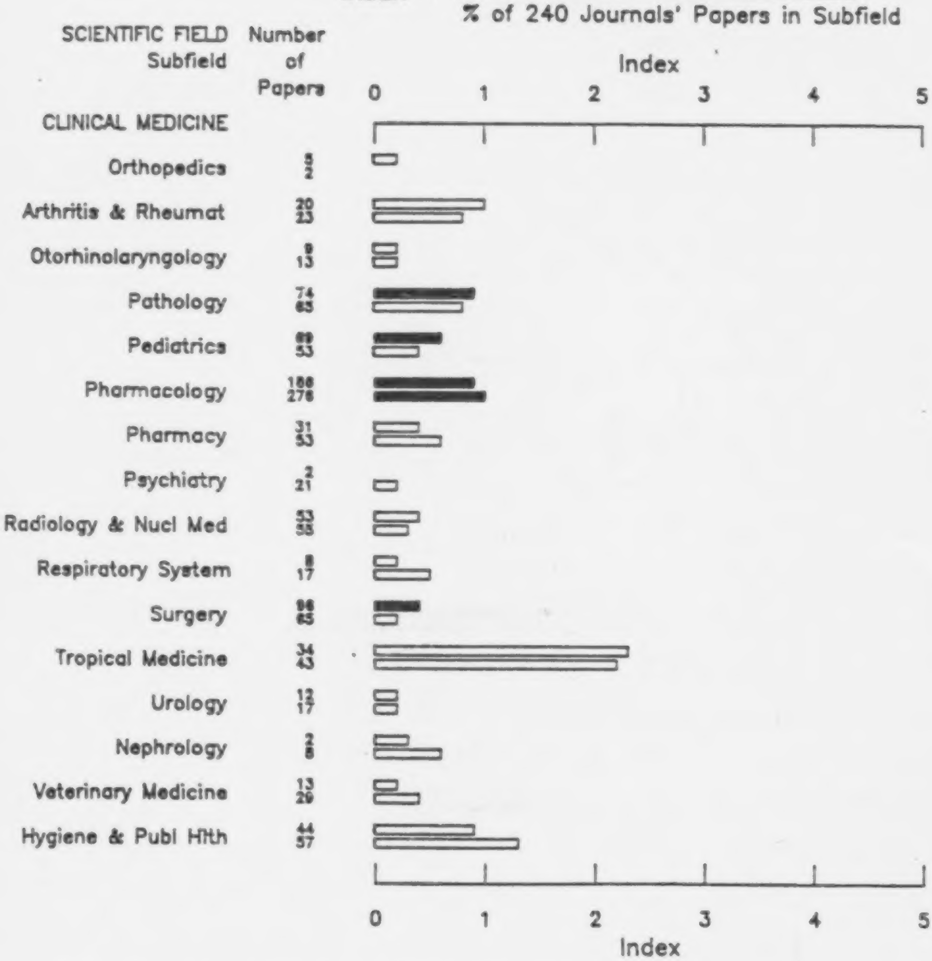
Note: Open bars designate subfields that contained less than 1 percent of the papers by intramural NIH authors in the given period.

Figure 12A (Continued)

NIH Intramural Activity Indexes in Subfields of Clinical Medicine

240 BID–MEDLINE Journals
1973–1976 over 1977–1980

$$\text{INDEX} = \frac{\text{\% of Institute's Papers in Subfield}}{\text{\% of 240 Journals' Papers in Subfield}}$$



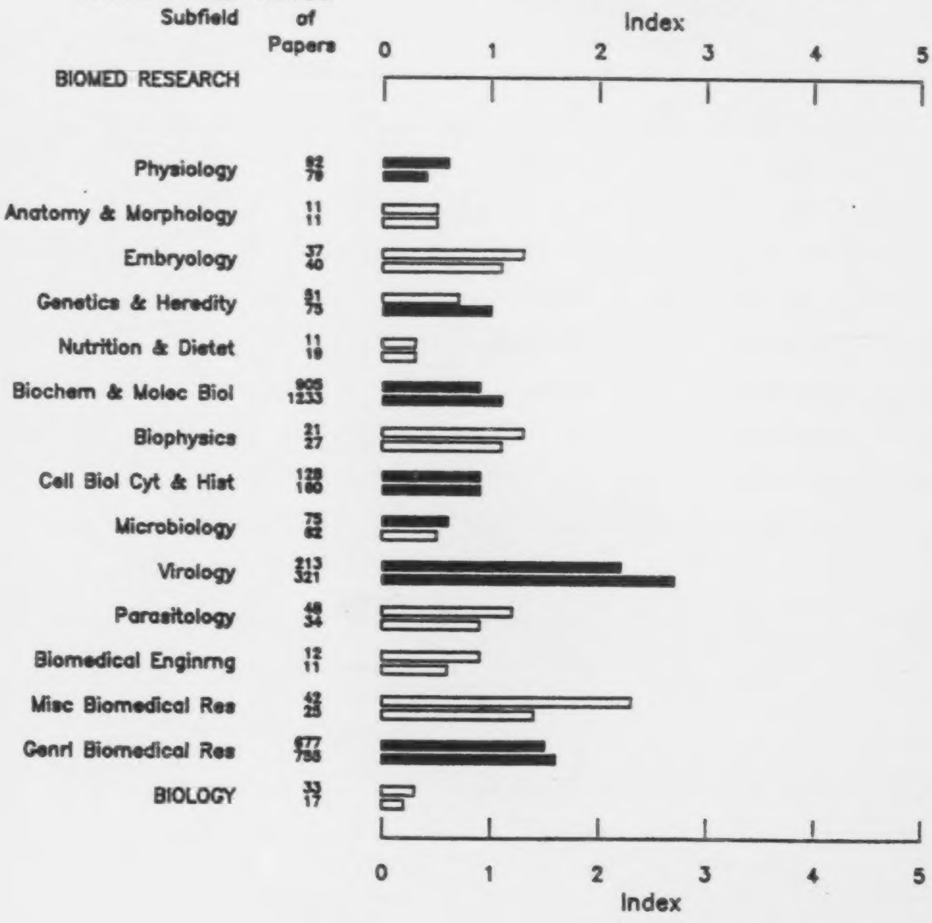
Note: Open bars designate subfields that contained less than 1 percent of the papers by intramural NIH authors in the given period.

Figure 12B

NIH Intramural Activity Indexes in Subfields of Biomedical Research

240 BID–MEDLINE Journals
1973–1976 over 1977–1980

$$\text{INDEX} = \frac{\text{\% of Institute's Papers in Subfield}}{\text{\% of 240 Journals' Papers in Subfield}}$$



Note: Open bars designate subfields that contained less than 1 percent of the papers by intramural NIH authors in the given period.

CITATION PERFORMANCE OF INTRAMURAL PAPERS

It is widely accepted within the research community that high citation rates are associated with quality research, especially when

- statistically meaningful numbers of papers are under scrutiny, and
- adequate normalization is supplied, to take account of differences between citation density in different subfields and periods.

Also widely accepted is the view that the very highly cited papers play a particularly important role in research advance.

Within the 240-journal database,

- 26.1 percent of the NIH intramural papers are in the top citation decile,
- 16.3 percent of NIH-supported extramural papers are in this decile,
- 11.7 percent of all other U.S.-supported papers are in the decile, and
- only 3.9 percent of the U.S. papers that do not acknowledge support are in the decile.

A paper is placed in the top citation decile if it is cited at least as frequently as the most frequently cited 10 percent of all papers in the field or subfield. For example, if 11 percent of the papers in a subfield are cited more than five times in a given year, then any paper cited more than five times in that year would be considered a "top decile" paper. Since citation counts are integer, the top decile always contains slightly more than 10 percent of the papers. For example, 10.64 percent of the papers in the entire database taken together are in the top decile.

The outstanding performance of the NIH intramural program is clearly apparent. More than two and one-half times as many NIH intramural papers are in the top 10 percent of cited papers in biomedicine as one would expect. Also, the citation performance of the NIH-supported extramural papers is excellent, with 60 percent more papers in the top decile then one would expect.

At the other end of the citation spectrum are the papers designated U.S. unacknowledged support--papers that did not have any kind of research support acknowledgement. These are usually clinical observation papers, written by a physician or other scientist without any outside funding. Only one-third as many of these are in the top decile, an indication that they are generally not in the mainstream of biomedical research.

Subfield Basis

The outstanding intramural publication record is not confined to any one subfield, but is virtually across the board. High citation counts are found in all the subfields in which NIH intramural papers are published. Before discussing the subfield results, a subtle point about the data should be clarified.

When top decile is defined on a subfield-by-subfield basis, the citation cutoff is different in each subfield. As a result, the average top decile percentages are slightly different from the ones previously given for all subfields combined. Specifically, within the 240 biomedical journals in our BID-MEDLINE database, on a subfield-by-subfield basis,

- 21.9 percent of the NIH intramural papers are in the top citation deciles of their subfields,
- 15.3 percent of the NIH-supported extramural papers are in these top citation deciles,
- 12.4 percent of all U.S.-authored and U.S.-supported papers are in these deciles, and
- only 7.3 percent of the U.S. papers with support unacknowledged are in these deciles.

The fact that the NIH intramural performance is not quite as high on a subfield-by-subfield basis, and the support-unacknowledged performance not quite as poor, are results of an interesting aspect of the data: NIH intramural papers are being published in the most highly cited subfields; the support-unacknowledged papers, in the least highly cited. As a result, a subfield-by-subfield comparison, while catching the breadth of the NIH performance, tends to underestimate the impact of these papers on biomedicine as a whole.

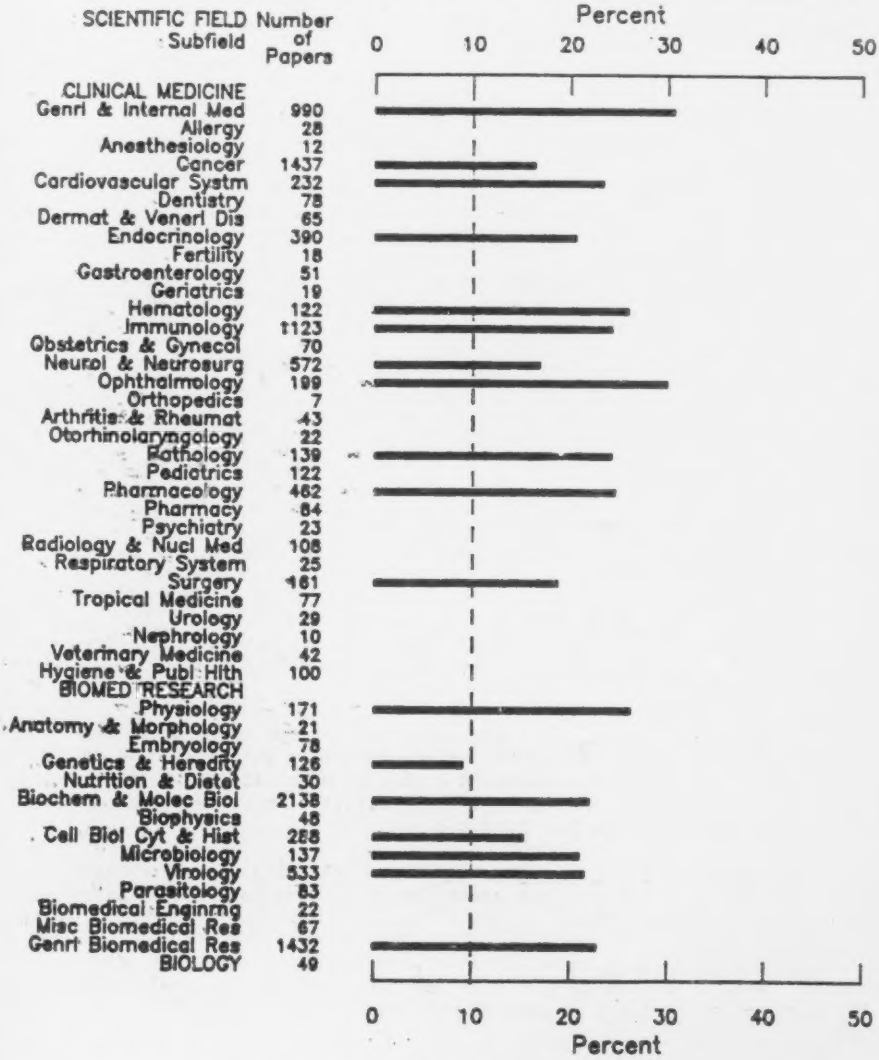
Figure 13 presents citation performance data for NIH intramural program publications subfield by subfield.

There are 18 biomedical subfields in which the NIH intramural program publishes more than one percent of its papers. In 17 of these subfields, substantially more than 10 percent of the papers are in the top decile. In only one subfield--Genetics and Heredity--is this not quite true. In the other 17 subfields, 15 percent or more of the NIH intramural papers are in the top decile, and in General and Internal Medicine and Ophthalmology, an almost incredible 30 percent of the NIH intramural papers are in the top decile of cited papers.

Figure 13

NIH Intramural

Percent of BID's Papers in Top Decile of Cited Papers
1973–1980 Papers in 240 BID–MEDLINE Journals



NOTE: No values shown for scientific subfields with less than 1 percent of papers for this BID.

INTRAMURAL PUBLICATION PROFILE

Just as Tables 5A and B presented bibliometric data for all NIH programs, Tables 9A and B are profiles of the bibliometric activity of the NIH Intramural Research Program (IRP).* Table 9A counts all papers published in the 240 BID-MEDLINE journal set in the years 1973-76 and counts citations received by these papers from the 275-journal set from 1973 through 1980. Table 9B is a profile of the NIH IRP for the period 1977-80.

The first page of each table presents the data for all fields combined, for each research level, and for each of the major fields. The second page lists the individual subfields of clinical medicine and biomedical research. The column headings, as in Tables 5A and B, are defined as follows:

1 Number of Papers - The fractional number of papers supported by this BID in the particular level, field, and subfield (L/F/S).

2 Activity Index - Proportion of the BID's papers in the L/F/S divided by the proportion of all papers in the BID-MEDLINE journal set in that L/F/S.

3 % Internal Effort - Percent of the BID's papers in the particular L/F/S.

4 % External Effort - Percent of all papers in the BID-MEDLINE journal set in the particular L/F/S that were supported by this BID.

5 Total Cites - Total citations (from all journals in the BID-MEDLINE set for citing years 1973-80) received by the papers supported by this BID in the particular L/F/S. Scaled to the average citation rate for each L/F/S in 1973.

6 Cites per Paper - Total scaled citations received by this BID's papers in a given L/F/S, divided by the number of papers supported.

7 Cite T-Score - This BID's average citations per paper minus the average citations per paper for all papers in the particular L/F/S, divided by the standard deviation of citations per paper for all papers in that L/F/S. The statistic is scaled to a mean of 50 and a standard deviation of 10.

8 % Papers Among the Top 10% - Percent of this BID's papers in the particular L/F/S that are among the 10 percent most highly cited papers in that L/F/S.

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*Again, the data are likely to be unstable when based on aggregates of less than 25. Because of skewness of citation distributions, a sample size of 20 is required to achieve a 95 percent confidence interval of ±2 citations.

Table 9A

BIBLIOMETRIC PROFILE OF NIH INTRAMURAL RESEARCH, 1973-76*

FIELD/LEVEL	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
************************ NORMALIZED AGAINST FIELDS [1-2] ************************								
FIELDS [1-2]	5521.	1.00	100.00	2.68	104466.	18.9	56.86	23.73
CLIN MEDICINE [1]	3198.	0.96	57.93	2.58	48973.	15.3	59.42	25.78
BIOMED RESEARCH [2]	2323.	1.06	42.07	2.83	55597.	23.9	55.88	23.89
LEVEL								
CLINICAL-MIX [1-2]	1209.	0.66	21.89	1.77	15642.	12.9	60.95	27.08
CLIN INVESTIGATN [3]	1887.	1.48	34.18	3.76	30751.	16.3	58.19	22.52
BASIC RESEARCH [4]	2425.	1.03	43.93	2.77	58043.	23.9	55.88	23.54
************************ NORMALIZED AGAINST FIELDS [1-9] ************************								
FIELDS [1-9]	5616.	1.00	100.00	2.53	104955.	18.7	57.23	24.93
CLIN MEDICINE [1]	3198.	1.02	56.95	2.58	48973.	15.3	59.42	25.78
BIOMED RESEARCH [2]	2323.	1.12	41.36	2.83	55597.	23.9	55.88	23.89
BIOLOGY [3]	33.	0.28	0.58	0.71	168.	5.1	52.83	19.29
CHEMISTRY [4]	49.	0.53	0.87	1.34	573.	11.7	57.39	23.13
PHYSICS [5]	1.	0.09	0.02	0.23	1.	1.0	40.80	0.00
EARTH & SPACE SC [6]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
ENGRNG & TECHNOL [7]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
PSYCHOLOGY [8]	12.	0.07	0.21	0.17	44.	3.6	52.58	25.00
MATHEMATICS [9]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00

NOTE: CHEMISTRY AND PSYCHOLOGY DATA SHOULD BE TREATED CAUTIOUSLY OVER TIME DUE TO INCONSISTENT DATABASE COVERAGE.

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*BID-SCI journal set citing BID-MEDLINE papers, 1973-80. Activity index normalized against Fields 1 and 2. Citation counts scaled within subfield to 1973 equivalents.

Table 9A (Continued)

BIBLIOMETRIC PROFILE OF NIH
INTRAMURAL RESEARCH, 1973-76*

FIELD/SUBFIELD	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
CLIN MEDICINE [1]								
GENRL & INTERNAL MED	489.	0.98	8.85	2.63	10830.	22.2	64.08	30.21
ALLERGY	13.	1.38	0.23	3.69	87.	6.8	48.82	7.79
ANESTHESIOLOGY	5.	0.13	0.09	0.35	9.	1.8	44.76	0.00
CANCER	673.	3.32	12.19	8.91	9975.	14.8	53.38	15.48
CARDIOVASCULAR SYSTM	119.	0.81	2.16	2.17	2262.	19.0	59.42	20.95
DENTISTRY	40.	0.42	0.72	1.13	189.	4.8	55.88	22.27
DERMAT & VENERL DIS	33.	0.94	0.60	2.51	207.	6.3	60.45	27.14
ENDOCRINOLOGY	168.	1.00	3.05	2.67	2721.	16.2	57.66	16.93
FERTILITY	9.	0.18	0.16	0.47	51.	5.7	52.36	16.67
GASTROENTEROLOGY	20.	0.45	0.36	1.21	297.	15.0	67.70	26.05
GERIATRICS	11.	0.28	0.19	0.76	37.	3.5	57.18	23.81
HEMATOLOGY	68.	1.13	1.23	3.02	878.	12.9	61.19	30.07
IMMUNOLOGY	469.	2.11	8.49	5.66	10552.	22.5	58.43	23.51
OBSTETRICS & GYNECOL	34.	0.40	0.61	1.08	285.	8.4	55.46	21.67
NEUROL & NEUROSURG	288.	0.90	5.22	2.42	3683.	12.8	52.48	15.55
OPHTHALMOLOGY	104.	1.37	1.89	3.67	949.	9.1	61.11	31.68
ORTHOPEDICS	5.	0.22	0.09	0.69	26.	5.4	54.90	20.69
ARTHRITIS & RHEUMAT	20.	1.01	0.36	2.72	272.	13.6	62.72	27.50
OTORHINOLARYNGOLOGY	9.	0.17	0.16	0.45	23.	2.6	49.63	16.98
PATHOLOGY	74.	0.95	1.33	2.53	778.	10.6	60.03	26.30
PEDIATRICS	69.	0.62	1.24	1.67	591.	8.6	58.62	21.65
PHARMACOLOGY	186.	0.90	3.37	2.42	3085.	16.6	58.31	25.72
PHARMACY	31.	0.38	0.56	1.02	236.	7.7	56.54	14.59
PSYCHIATRY	2.	0.02	0.04	0.07	23.	10.8	62.80	23.08
RADIOLOGY & NUCL MED	53.	0.45	0.95	1.21	313.	5.9	52.36	12.03
RESPIRATORY SYSTEM	8.	0.23	0.14	0.61	158.	19.7	72.20	60.42
SURGERY	96.	0.40	1.74	1.06	630.	6.6	53.41	17.91
TROPICAL MEDICINE	34.	2.28	0.62	6.12	157.	4.6	53.53	19.12
UROLOGY	12.	0.21	0.21	0.56	60.	5.1	55.26	23.94
NEPHROLOGY	2.	0.26	0.04	0.69	30.	14.9	73.07	50.00
VETERINARY MEDICINE	13.	0.25	0.24	0.66	47.	3.6	53.26	22.78
ADDICTIVE DISEASES	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
HYGIENE & PUBL HLTH	44.	0.85	0.79	2.28	245.	5.6	59.39	21.84
BIOMED RESEARCH [2]								
PHYSIOLOGY	92.	0.64	1.66	1.71	2090.	22.8	58.17	26.23
ANATOMY & MORPHOLOGY	11.	0.49	0.19	1.30	37.	3.5	45.59	0.00
EMBRYOLOGY	37.	1.27	0.68	3.41	584.	15.6	59.45	20.09
GENETICS & HEREDITY	51.	0.74	0.93	1.98	459.	8.9	50.01	9.09
NUTRITION & DIETET	11.	0.29	0.20	0.77	79.	7.1	51.95	18.18
BIOCHEM & MOLEC BIOL	905.	0.93	16.38	2.50	22443.	24.8	54.72	22.92
BIOPHYSICS	21.	1.28	0.38	3.43	174.	8.3	54.29	19.20
CELL BIOL CYT & HIST	128.	0.88	2.32	2.36	2462.	19.2	54.11	13.12
MICROBIOLOGY	75.	0.57	1.35	1.52	715.	9.6	53.69	20.76
VIROLOGY	213.	2.18	3.85	5.83	6179.	29.1	62.62	24.92
PARASITOLOGY	48.	1.22	0.88	3.27	185.	3.8	52.99	15.52
BIOMEDICAL ENGINRNG	12.	0.88	0.21	2.35	58.	4.9	64.78	36.62
MISC BIOMEDICAL RES	42.	2.29	0.77	6.14	80.	1.9	50.62	12.99
GENRL BIOMEDICAL RES	677.	1.46	12.27	3.92	19784.	29.2	57.10	22.81

Table 9B

BIBLIOMETRIC PROFILE OF NIH INTRAMURAL RESEARCH, 1977-80*

FIELD/LEVEL	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
************************ NORMALIZED AGAINST FIELDS [1-2] ************************								
FIELDS [1-2]	6510.	1.00	100.00	2.84	60065.	19.4	59.53	26.94
CLIN MEDICINE [1]	3660.	0.92	56.22	2.61	28783.	16.2	62.05	29.41
BIOMED RESEARCH [2]	2850.	1.13	43.78	3.20	31077.	23.3	58.46	24.13
LEVEL								
CLINICAL-MIX [1-2]	1258.	0.58	19.33	1.63	8892.	13.7	61.46	29.72
CLIN INVESTIGATN [3]	2272.	1.41	34.90	4.00	18503.	17.4	62.06	25.93
BASIC RESEARCH [4]	2980.	1.10	45.77	3.12	32355.	23.2	58.49	23.80
************************ NORMALIZED AGAINST FIELDS [1-9] ************************								
FIELDS [1-9]	6577.	1.00	100.00	2.75	59326.	18.9	59.79	28.05
CLIN MEDICINE [1]	3660.	0.95	55.65	2.61	28783.	16.2	62.05	29.41
BIOMED RESEARCH [2]	2850.	1.16	43.34	3.20	31077.	23.3	58.46	24.13
BIOLOGY [3]	17.	0.19	0.25	0.53	19.	3.8	49.41	20.00
CHEMISTRY [4]	44.	0.58	0.67	1.59	312.	12.1	57.50	26.62
PHYSICS [5]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
EARTH & SPACE SC [6]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
ENGRNG & TECHNOL [7]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
PSYCHOLOGY [8]	5.	0.05	0.08	0.15	5.	1.1	45.37	7.41
MATHEMATICS [9]	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00

NOTE: CHEMISTRY AND PSYCHOLOGY DATA SHOULD BE TREATED CAUTIOUSLY OVER TIME DUE TO INCONSISTENT DATABASE COVERAGE.

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*BID-SCI journal set citing BID-MEDLINE papers, 1973-80, but does not include citations received by 1979-80 publications. Activity index normalized against Fields 1 and 2. Citation counts scaled within subfield to 1973 equivalents.

Table 9B (Continued)

BIBLIOMETRIC PROFILE OF NIH
INTRAMURAL RESEARCH, 1977-80*

FIELD/SUBFIELD	NUMBER PAPERS	ACTIV INDEX	% INT EFFRT	% EXT EFFRT	TOTAL CITES	CITES PER PAPER	CITE T-SCR	% PAPERS AMONG TOP 10%
CLIN MEDICINE [1]								
GENRL & INTERNAL MED	501.	0.92	7.70	2.61	6199.	23.5	63.80	31.21
ALLERGY	16.	1.16	0.24	3.30	87.	13.5	65.45	30.77
ANESTHESIOLOGY	7.	0.18	0.11	0.52	22.	6.2	56.60	42.86
CANCER	764.	2.80	11.74	7.96	6504.	16.2	56.00	17.60
CARDIOVASCULAR SYSTM	113.	0.67	1.73	1.91	1019.	23.0	67.58	29.70
DENTISTRY	39.	0.37	0.59	1.06	67.	3.0	50.52	17.42
DERMAT & VENERL DIS	32.	0.70	0.49	2.00	252.	14.4	77.71	47.62
ENDOCRINOLOGY	221.	1.16	3.40	3.31	1747.	20.8	70.99	27.63
FERTILITY	9.	0.16	0.13	0.46	2.	1.8	44.10	0.00
GASTROENTEROLOGY	31.	0.54	0.47	1.53	207.	12.6	74.52	24.24
GERIATRICS	8.	0.26	0.13	0.73	8.	1.5	48.94	12.90
HEMATOLOGY	54.	0.73	0.83	2.08	251.	8.8	62.93	15.79
IMMUNOLOGY	654.	2.19	10.05	6.21	6868.	21.9	67.04	25.35
OBSTETRICS & GYNECOL	36.	0.37	0.55	1.06	159.	8.1	54.85	15.25
NEUROL & NEUROSURG	283.	0.69	4.35	1.96	1944.	13.5	55.15	19.42
OPHTHALMOLOGY	95.	1.10	1.46	3.11	414.	8.9	58.56	26.07
ORTHOPEDICS	2.	0.05	0.03	0.13	0.	0.0	0.00	0.00
ARTHRITIS & RHEUMAT	23.	0.77	0.35	2.19	223.	38.2	93.97	51.43
OTORHINOLARYNGOLOGY	13.	0.24	0.20	0.67	0.	0.0	42.56	0.00
PATHOLOGY	65.	0.76	1.00	2.17	258.	8.1	56.35	19.37
PEDIATRICS	53.	0.35	0.81	1.00	202.	7.7	55.21	29.75
PHARMACOLOGY	276.	1.04	4.23	2.96	1520.	15.0	56.47	22.61
PHARMACY	53.	0.60	0.81	1.70	240.	8.5	58.75	24.85
PSYCHIATRY	21.	0.22	0.33	0.61	104.	8.3	58.67	28.00
RADIOLOGY & NUCL MED	55.	0.34	0.85	0.97	204.	10.5	58.93	30.77
RESPIRATORY SYSTEM	17.	0.47	0.27	1.33	78.	11.4	81.59	19.51
SURGERY	65.	0.25	0.99	0.70	292.	7.8	55.17	20.88
TROPICAL MEDICINE	43.	2.16	0.66	6.14	191.	7.2	60.87	28.48
UROLOGY	17.	0.25	0.26	0.71	115.	12.5	75.82	36.36
NEPHROLOGY	8.	0.62	0.12	1.77	0.	0.0	0.00	0.00
VETERINARY MEDICINE	29.	0.36	0.45	1.03	53.	3.3	52.05	12.24
ADDICTIVE DISEASES	0.	0.00	0.00	0.00	0.	0.0	0.00	0.00
HYGIENE & PUBL HLTH	57.	1.27	0.87	3.60	125.	5.0	57.00	26.17
BIOMED RESEARCH [2]								
PHYSIOLOGY	79.	0.43	1.21	1.23	961.	23.8	62.21	26.03
ANATOMY & MORPHOLOGY	11.	0.46	0.16	1.30	6.	1.3	36.40	0.00
EMBRYOLOGY	40.	1.07	0.62	3.04	160.	7.4	37.90	6.15
GENETICS & HEREDITY	75.	0.95	1.15	2.71	249.	9.1	50.94	9.15
NUTRITION & DIETET	19.	0.29	0.29	0.83	70.	5.9	48.40	0.00
BIOCHEM & MOLEC BIOL	1233.	1.07	18.94	3.04	12680.	22.4	57.02	20.48
BIOPHYSICS	27.	1.08	0.42	3.06	29.	7.8	52.06	22.06
CELL BIOL CYT & HIST	160.	0.94	2.45	2.67	1416.	19.2	58.48	19.23
MICROBIOLOGY	62.	0.50	0.95	1.43	334.	11.4	58.72	21.59
VIROLOGY	321.	2.68	4.92	7.61	3409.	21.6	68.54	16.91
PARASITOLOGY	34.	0.88	0.53	2.49	69.	4.4	54.49	19.35
BIOMEDICAL ENGINRNG	11.	0.61	0.16	1.74	41.	5.8	69.72	42.86
MISC BIOMEDICAL RES	25.	1.41	0.38	3.99	14.	1.1	46.64	11.69
GENRL BIOMEDICAL RES	755.	1.57	11.60	4.45	10465.	29.6	59.44	22.74

SUMMARY

Bibliometrics, the development and analysis of data on publication, provides a reliable method for assessing support activity in biomedical research programs. This report applies bibliometric techniques to NIH-supported publications from 1973 to 1980 in 240 selected journals--the "BID-MEDLINE data set." Part I covers NIH as a whole, Part II the intramural research program.

As one application of bibliometrics, Part I compares funding and publication, both for papers supported by NIH totally and by the component InInstitutes. For NIH as a whole the correlation is very high, r = .90, when funds for 1965-77 are compared with publications three years later. For most of the individual Institutes, the values ranged between .70 and .95.

Between 1970 and 1980 total NIH-supported papers increased 30 percent and total BID-MEDLINE papers increased 40 percent. The most notable change in the distribution of papers was an increase in foreign papers that received no NIH support from 29.6 percent of the journal set to 32.9 percent.

When publications are classified by research level for two periods, 1973-76 and 1977-80, NIH is seen to have supported modest increases in basic research (14.5 percent) and clinical investigation (8.7 percent). More clinically oriented papers declined slightly (4.1 percent).

NIH supported a substantial number of papers in nearly every subfield. In Cancer and Immunology, NIH supported more than 40 percent of the total 1973-80 BID-MEDLINE papers. It supported more than 30 percent of all papers in seven other subfields.

NIH's "activity index"--a measure of NIH-supported publications in a subfield in relation to all publication in that subfield--was highest for Cancer: 1.59 in 1977-80, or 1.59 times the "expected" level. The other subfields in which the index for 1977-80 was higher than 1 (and publication exceeded 2,000 papers) were Endocrinology, Immunology, Physiology, Biochemistry, Molecular Biology, Cell Biology-Cytology-Histology, and General Biomedical Research.

Between 1973-76 and 1977-80, NIH support, as compared with other U.S., decreased notably in the clinical subfields Anesthesiology, Dermatology-Venereal Diseases, Otorhinolaryngology, and Surgery. All U.S. publication decreased in Geriatrics and Fertility. In contrast, NIH publications increased substantially relative to the rest of the U.S. in the subfields of Physiology, Immunology, Hematology, Biophysics, Respiratory System, Virology, Pharmacology, and Biochemistry-Molecular Biology. In several clinical subfields, NIH increases lagged well behind the rest of the U.S.--Allergy, Orthopedics, Arthritis, Pediatrics, Nephrology, and Nutrition-Dietetics.

NIH's record of supporting outstanding investigators is manifest in citations of NIH publications. In each of the 21 subfields in which NIH was most active over the entire period, more than 10 percent of the NIH-supported papers were in the top decile of cited papers. Indeed, over 10 percent of the papers in each of the subfields in which NIH supported any papers were in the top decile.

That the Institutes and other support sources are interdependent in their research is clear from interaction in citation. While 52 percent of the references in NIH-supported papers were to research supported by NIH, 48 percent were to research supported by others. Conversely, 54 percent of the citations of NIH research were in papers with other than NIH support. NIH receives 23 percent of its citations from foreign papers.

Publication profiles for NIH summarize its bibliometric activity for 1973-76 and 1977-80.

The crosscutting scientific interests of NIH programs are demonstrated. Clinical and basic disciplines that were substantially supported by more than one Institute are listed. In each of 14 disciplines, only one Institute was substantially involved. Predictably, all Institutes supported a substantial activity in Biochemistry and Molecular Biology.

Finally, Appendix A lists the 10 most highly cited NIH-supported papers and NIH intramural papers published each year from 1973 to 1977. Similarly, Appendix B lists papers published during those years by all U.S. and U.S.-supported authors, U.S. authors with non-Federal support, U.S. authors who did not acknowledge support, and foreign authors.

An analysis comparable to that represented above is given for the NIH Intramural Research Program (IRP), which accounts for about 10 percent of NIH-supported publications. Again, there is a strong correlation between obligations and number of papers published three years later ($r = .93$).

Between 1973-76 and 1977-80, the percent, but not number, of IRP papers at the most clinical levels decreased, whereas papers at the more basic levels--clinical investigation and basic research--increased in both number and percent.

The IRP and NIH altogether play a major support role in most clinical and basic research subfields, with 10 to 50 percent of the papers in all but two subfields acknowledging NIH support. The areas of greatest relative emphasis, for both NIH and the IRP, are Cancer, Virology, and Immunology. The activity indexes for these fields were 2.80, 2.68, and 2.19.

Citation of NIH-supported papers is analyzed for the period 1973-80. Among IRP papers, 26 percent were in the top citation decile. Sixteen percent of grantee papers were in that decile. This outstanding publication record virtually extends across the board of subfields. In the top citation deciles of their subfields were nearly 22 percent of the IRP papers and 15 percent of the grantee papers.

Complete publication profiles of the IRP are presented.

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APPENDIX A

THE TEN MOST HIGHLY CITED PAPERS SUPPORTED BY NIH AND BY THE NIH INTRAMURAL PROGRAM

Appendix A provides information about highly cited individual papers. The 10 most highly cited papers supported by NIH in each year, 1973 through 1977, are listed in these tables. These are papers in the BIO-MEDLINE data base, cited by 1973-80 papers. Since the 1978, 1979, and 1980 papers have less than three full years of citations attributed to them (by 1980), they are not included in these tables.

Lists of the 25 most highly cited papers supported by each Institute, and of the 25 most highly cited in each subfield and at each research level, for the years 1973 through 1977, are available in the Program Evaluation Branch, OD, NIH (phone: 301/496-4418). Information provided in these lists includes citation frequency rank, the number of citations received each year from 1973 through 1980, journal identification, authors, title, L/F/S (level, field, subfield), institutional affiliations of authors, and acknowledged support sources.

See also Appendix B for lists of the 10 most highly cited papers published each year from 1973 through 1977 in four categories: (1) U.S.-authored and -supported papers, (2) U.S. papers with non-Federal support, (3) U.S. papers with support unacknowledged, and (4) foreign papers.

APPENDIX A

Table 1

The Ten 1973 NIH-Supported Papers Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
1	598	0	64	81	95	102	95	94	67	DETECTION OF TWO RESTRICTION ENDONUCLEASE ACTIVITIES IN HAEMOPHILUS PARAINFLUENZAE USING ANALYTICAL AGAROSE--ETHIDIUM BROMIDE ELECTROPHORESIS. By: SHARP PA ; SUGDEN B ; SAMBROOK J In: BIOCHEMISTRY 12(16):3055-63, 31 JUL 73 Support source(s): CANCER INSTITUTE Corporate Address: COLD SP HRBR LAB
2	460	3	24	70	74	78	77	61	73	MICROTUBULE ASSEMBLY IN THE ABSENCE OF ADDED NUCLEOTIDES. By: SHELANSKI ML ; GASKIN F ; CANTOR CR In: PROC NATL ACAD SCI USA 70(3):765-8, MAR 73 Support source(s): HEART,LUNG, & BLOOD INSTITUTE NEUROL DISEASES & STROKE GENERAL MEDICAL SCIENCES Corporate Address: COLUMBIA, NYC NIH
3	396	5	43	42	66	73	62	48	57	CELLULAR LOCALIZATION OF AN FPSTEIN-BARR VIRUS (EBV)-ASSOCIATED COMPLEMENT-FIXING ANTIGEN IN PRODUCER AND NON-PRODUCER LYMPHOBLASTOID CELL LINES. By: REEDMAN BM ; KLEIN G In: INT J CANCER 11(3):499-520, MAY 73 Support source(s): CANCER INSTITUTE Corporate Address: FOREIGN
4	339	2	49	53	58	53	51	42	31	THE BIOCHEMISTRY OF PLANT LECTINS (PHYTOHEMAGGLUTININS). By: LIS H ; SHARON N In: ANNU REV BIOCHEM 42(0):541-74, 1973 Support source(s): LIBRARY OF MEDICINE NATL INSTITUTE OF HEALTH-GENL DEPT OF AGRICULTURE Corporate Address: FOREIGN
5	321	0	15	27	38	52	64	63	62	MATURATION OF THE HEAD OF BACTERIOPHAGE T4. I. DNA PACKAGING EVENTS. By: LAEMMLI UK ; FAVRE M In: J MOL BIOL 80(4):575-99, 15 NOV 73 Support source(s): GENERAL MEDICAL SCIENCES Corporate Address: PRINCETON U

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 1 (Continued)

The Ten 1973 NIH-Supported Papers
Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
6	263	3	20	23	33	43	49	47	45	A HOMOLOGOUS RADIOIMMUNOASSAY FOR HUMAN PROLACTIN. By: SINHA YN ; SELBY FW ; LEWIS UJ ; VANDERLAAN WP In: J CLIN ENDOCRINOL METAB 36(3):509-16, MAR 73 Support source(s): ARTHR & METABOL DIS AMERICAN CANCER SOCIETY Corporate Address: SCRIPPS CLINIC
7	246	5	23	23	35	43	40	31	46	AN ENZYMATIC FUNCTION ASSOCIATED WITH TRANSFORMATION OF FIBROBLASTS BY ONCOGENIC VIRUSES. I. CHICK EMBRYO FIBROBLAST CULTURES TRANSFORMED BY AVIAN RNA TUMOR VIRUSES. By: UNKELESS JC ; TOBIA A ; OSSOWSKI L ; QUIGLEY JP ; RIFKIN DB REICH E In: J EXP MED 137(1):85-111, 1 JAN 73 Support source(s): AMERICAN CANCER SOCIETY CANCER INSTITUTE Corporate Address: ROCKFLR U, NY
8	245	3	30	33	41	29	45	27	37	EVIDENCE FOR RECYCLING OF SYNAPTIC VESICLE MEMBRANE DURING TRANSMITTER RELEASE AT THE FROG NEUROMUSCULAR JUNCTION. By: HEUSER JE ; REESE TS In: J CELL BIOL 57(2):315-44, MAY 73 Support source(s): NEUROL DISEASES & STROKE Corporate Address: NIH
9	241	1	13	37	37	34	32	44	43	FUNCTION OF MACROPHAGES IN ANTIGEN RECOGNITION BY GUINEA PIG T LYMPHOCYTES. I. REQUIREMENT FOR HISTOCOMPATIBLE MACROPHAGES AND LYMPHOCYTES. By: ROSENTHAL AS ; SHEVACH EM In: J EXP MED 138(5):1194-212, 1 NOV 73 Support source(s): ALLERG & INFECT DISEASES Corporate Address: NIH
10	231	1	16	34	23	33	37	43	44	BIOLOGICAL DEFENSE MECHANISMS. THE PRODUCTION BY LEUKOCYTES OF SUPEROXIDE, A POTENTIAL BACTERICIDAL AGENT. By: BABIOR BM ; KIPNES RS ; CURNUTTE JT In: J CLIN INVEST 52(3):711-4, MAR 73 Support source(s): ARTHR & METABOL DIS DIV RESCH FACIL & RESOURCES Corporate Address: HARVARD MED

APPENDIX A

Table 1 (Continued)

The Ten 1973 NIH-Supported Papers
Most Highly Cited in 1973-80*

	Total Cites	Cites received by citing year								
Rank	Received	73	74	75	76	77	78	79	80	
10	231	0	17	35	44	33	38	40	24	MICROFLUOROMETRIC DETECTION OF DEOXYRIBONUCLEIC ACID REPLICATION IN HUMAN METAPHASE CHROMOSOMES. By: LATT SA In: PROC NATL ACAD SCI USA 70(12):3395-9, DEC 73 Support source(s): CHILD HEALTH & HUMAN DEV Corporate Address: CHL HOS MED CTR HARVARD MED

APPENDIX A

Table 2

The Ten 1974 NIH-Supported Papers Most Highly Cited in 1974-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
		Cites received by citing year								
1	649		8	30	81	96	125	133	176	A HIGHLY SENSITIVE ADENYLATE CYCLASE ASSAY. By: SALOMON Y ; LONDOS C ; RODBELL M In: ANAL BIOCHEM 58(2):541-8, APR 74 Support source(s): ARTHR & METABOL DIS DENTAL RESEARCH Corporate Address: NIH
2	375		0	11	48	64	79	91	82	A SIMPLIFIED METHOD FOR CYANOGEN BROMIDE ACTIVATION OF AGAROSE FOR AFFINITY CHROMATOGRAPHY. By: MARCH SC ; PARIKH I ; CUATRECASAS P In: ANAL BIOCHEM 60(1):149-52, JUL 74 Support source(s): ARTHR & METABOL DIS GENERAL MEDICAL SCIENCES Corporate Address: JOHNS HOPKINS MED
3	346		5	51	71	98	54	47	20	SPHEROID CHROMATIN UNITS (V BODIES). By: OLINS AL ; OLINS DE In: SCIENCE 183(122):330-2, 25 JAN 74 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) GENERAL MEDICAL SCIENCES Corporate Address: U TENN, KNOXVLL OAK RIDGE LABS
4	344		11	44	63	67	72	48	39	PREDICTION OF PROTEIN CONFORMATION. By: CHOU PY ; FASMAN GD In: BIOCHEMISTRY 13(2):222-45, 15 JAN 74 Support source(s): GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION AMERICAN HEART ASSOC Corporate Address: BRANDEIS U, WALT
5	318		3	42	58	61	53	62	39	ARENE OXIDES: A NEW ASPECT OF DRUG METABOLISM. By: JERINA DM ; DALY JW In: SCIENCE 185(151):573-82, 16 AUG 74 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 2 (Continued)

The Ten 1974 NIH-Supported Papers
Most Highly Cited in 1974-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
		Cites received by citing year								
6	314		3	28	39	49	67	68	60	INSULIN-DEPENDENT REGULATION OF INSULIN RECEPTOR CONCENTRATIONS: A DIRECT DEMONSTRATION IN CELL CULTURE. By: GAVIN JR 3D ; ROTH J ; NEVILLE DM JR ; MEYTS P DE ; BUELL DN In: PROC NATL ACAD SCI USA 71(1):84-8, JAN 74 Support source(s): ARTHR & METABOL DIS CANCER INSTITUTE FOGARTY INTERNATL CENTER Corporate Address: NIH NIMH
7	237		1	35	58	36	41	38	28	MEMBRANE PECEPTORS. By: CUATRECASAS P In: ANNU REV BIOCHEM 43(0):169-214, 1974 Support source(s): ARTHR & METABOL DIS NATL SCIENCE FOUNDATION AMERICAN CANCER SOCIETY Corporate Address: JOHNS HOPKINS MED
8	230		4	28	39	42	34	40	43	ACTIN ANTIBODY: THE SPECIFIC VISUALIZATION OF ACTIN FILAMENTS IN NON-MUSCLE CELLS. By: LAZARIDES E ; WEBER K In: PROC NATL ACAD SCI USA 71(6):2268-72, JUN 74 Support source(s): CANCER INSTITUTE Corporate Address: COLD SP HRBR LAB
9	227		0	6	31	39	43	53	55	MAGNESIUM PRECIPITATION OF RIBONUCLEOPROTEIN COMPLEXES. EXPEDIENT TECHNIQUES FOR THE ISOLATION OF UNDERGRADED POLYSOMES AND MESSENGER RIBONUCLEIC ACID. By: PALMITER RD In: BIOCHEMISTRY 13(17):3606-15, 13 AUG 74 Support source(s): CHILD HEALTH & HUMAN DEV NATL SCIENCE FOUNDATION PRIVATE FOR PROFIT Corporate Address: HARVARD U, CMBRG
9	227		14	31	43	44	29	31	35	CONFORMATIONAL PARAMETERS FOR AMINO ACIDS IN HELICAL, BETA-SHEET, AND RANDOM COIL REGIONS CALCULATED FROM PROTEINS. By: CHOU PY ; FASMAN GD In: BIOCHEMISTRY 13(2):211-22, 15 JAN 74 Support source(s): GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION AMERICAN HEART ASSOC Corporate Address: BRANDEIS U, WALT

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Table 3

The Ten 1975 NIH-Supported Papers Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	554			0	9	34	93	201	217	RAPID ISOLATION OF ANTIGENS FROM CELLS WITH A STAPHYLOCOCCAL PROTEIN A-ANTIBODY ADSORBENT: PARAMETERS OF THE INTERACTION OF ANTIBODY-ANTIGEN COMPLEXES WITH PROTEIN A. By: KESSLER SW In: J IMMUNOL 115(6):1617-24, DEC 75 Support source(s): CANCER INSTITUTE Corporate Address: UCLA MED SCH
2	475			2	14	76	103	151	129	TRANSFER OF PROTEINS ACROSS MEMBRANES. I. PRESENCE OF PROTEOLYTICALLY PROCESSED AND UNPROCESSED NASCENT IMMUNOGLOBULIN LIGHT CHAINS ON MEMBRANE-BOUND RIBOSOMES OF MURINE MYELOMA. By: BLOBEL G ; DOBBERSTEIN B In: J CELL BIOL 67(3):835-51, DEC 75 Support source(s): CANCER INSTITUTE Corporate Address: ROCKFLR U, NY
3	333			5	60	72	62	66	68	FUNCTIONAL SUBCLASSES OF T-LYMPHOCYTES BEARING DIFFERENT LY ANTIGENS. I. THE GENERATION OF FUNCTIONALLY DISTINCT T-CELL SUBCLASSES IS A DIFFERENTIATIVE PROCESS INDEPENDENT OF ANTIGEN. By: CANTOR H ; BOYSE EA In: J EXP MED 141(6):1376-89, 1 JUN 75 Support source(s): CANCER INSTITUTE ALLERG & INFECT DISEASES Corporate Address: CHILDRENS CANC RES FDN SLOAN-KTRG CANC RES INST, NY
4	295			2	23	39	55	77	99	NUCLEOTIDE SEQUENCE OF THE RIGHTWARD OPERATOR OF PHAGE LAMBDA. By: MANIATIS T ; JEFFREY A ; KLEID DG In: PROC NATL ACAD SCI USA 72(3):1184-8, MAR 75 Support source(s): NATL SCIENCE FOUNDATION NATL INSTITUTE OF HEALTH-GENL Corporate Address: HARVARD U, CMBRG
5	285			3	15	59	67	74	67	CHAIN LENGTH DETERMINATION OF SMALL DOUBLE- AND SINGLE-STRANDED DNA MOLECULES BY POLYACRYLAMIDE GEL ELECTROPHORESIS. By: MANIATIS T ; JEFFREY A ; VAN DESANDE H In: BIOCHEMISTRY 14(17):3787-94, 26 AUG 75 Support source(s): NATL INSTITUTE OF HEALTH-GENL NATL SCIENCE FOUNDATION Corporate Address: HARVARD U, CMBRG MIT, CAMBRIDGE

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*BID-SCI Journal set citing BID-MEDLINE papers.

APPENDIX A

Table 3 (Continued)

The Ten 1975 NIH-Supported Papers
Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
6	282			6	55	51	49	60	61	FUNCTIONAL SUBCLASSES OF T LYMPHOCYTES BEARING DIFFERENT LY ANTIGENS. II. COOPERATION BETWEEN SUBCLASSES OF LY+ CELLS IN THE GENERATION OF KILLER ACTIVITY. By: CANTOR H ; BOYSE EA In: J EXP MED 141(6):1390-9, 1 JUN 75 Support source(s): CANCER INSTITUTE ALLERG & INFECT DISEASES Corporate Address: CHILDRENS CANC RES FDN SLOAN-KTRG CANC RES INST, NY
7	246			12	31	49	55	56	43	STUDIES ON THE CLEAVAGE OF BACTERIOPHAGE LAMBDA DNA WITH ECORI RESTRICTION ENDONUCLEASE. By: THOMAS M ; DAVIS RW In: J MOL BIOL 91(3):315-28, 25 JAN 75 Support source(s): GENERAL MEDICAL SCIENCES PRIVATE FOR PROFIT Corporate Address: STANFORD U MED
8	215			6	25	39	36	60	49	IDENTIFICATION OF A CALCIUM-BINDING PROTEIN AS A CALCIUM-DEPENDENT REGULATOR OF BRAIN ADENYLATE CYCLASE. By: BROSTROM CO ; HUANG YC ; BRECKENRIDGE BM ; WOLFF DJ In: PROC NATL ACAD SCI USA 72(1):64-8, JAN 75 Support source(s): NEUROL DISEASES & STROKE Corporate Address: RUTGERS U, N BRUN
9	214			1	27	46	39	52	49	THE SODIUM-POTASSIUM ADENOSINE TRIPHOSPHATASE: PHARMACOLOGICAL, PHYSIOLOGICAL AND BIOCHEMICAL ASPECTS. By: SCHWARTZ A ; LINDENMAYER GE ; ALLEN JC In: PHARMACOL REV 27(01):3-134, MAR 75 Support source(s): HEART,LUNG, & BLOOD INSTITUTE NATL INSTITUTE OF HEALTH-GENL AMERICAN HEART ASSOC Corporate Address: BAYLOR U, HOUSTON (MED) UNIDENTIFIED
10	203			3	51	37	36	49	27	BONE-MARROW TRANSPLANTATION (FIRST OF TWO PARTS). By: THOMAS E ; STORB R ; CLIFT RA ; FEFER A ; JOHNSON FL ; NEIMAN PE LERNER KG ; GLUCKSBERG H ; BUCKNER CD In: N ENGL J MED 292(16):832-43, 17 APR 75 Support source(s): CANCER INSTITUTE ALLERG & INFECT DISEASES AMERICAN CANCER SOCIETY Corporate Address: U WASH MED UNIDENTIFIED

APPENDIX A

Table 4

The Ten 1976 NIH-Supported Papers
Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	1077				0	30	140	360	547	A RAPID AND SENSITIVE METHOD FOR THE QUANTITATION OF MICROGRAM QUANTITIES OF PROTEIN UTILIZING THE PRINCIPLE OF PROTEIN-DYE BINDING. By: BRADFORD MM In: ANAL BIOCHEM 72:248-54, 7 MAY 76 Support source(s): CHILD HEALTH & HUMAN DEV FORD FOUNDATION Corporate Address: U GA, ATHENS
2	280				22	62	74	65	57	SURFACE MODULATION IN CELL RECOGNITION AND CELL GROWTH. By: EDELMAN GM In: SCIENCE 192(4236):218-26, 16 APR 76 Support source(s): ALLERG & INFECT DISEASES ARTHR & METABOL DIS CHILD HEALTH & HUMAN DEV Corporate Address: ROCKFLR U, NY
3	253				3	41	70	71	68	CELL SURFACE PROTEINS AND MALIGNANT TRANSFORMATION. By: HYNES RO In: BIOCHIM BIOPHYS ACTA 458(1):73-107, 30 APR 76 Support source(s): CANCER INSTITUTE Corporate Address: MIT, CAMBRIDGE
4	250				16	49	72	60	53	TRANSMEMBRANE CONTROL OF THE RECEPTORS ON NORMAL AND TUMOR CELLS. I. CYTOPLASMIC INFLUENCE OVER SURFACE COMPONENTS. By: NICOLSON GL In: BIOCHIM BIOPHYS ACTA 457(1):57-108, 13 APR 76 Support source(s): CANCER BIOL & DIAG - CANC INST NATL SCIENCE FOUNDATION CANCER INSTITUTE Corporate Address: U CAL, IRVINE SALK INST BIOL
5	236				4	43	58	74	57	THE ROLE OF POLYPRENOL-LINKED SUGARS IN GLYCOPROTEIN SYNTHESIS. By: WAECHTER CJ ; LENNARZ WJ In: ANNU REV BIOCHEM 45:95-112, 1976 Support source(s): NEUROL DISEASES & STROKE UNIV+MED SCHOOLS(STATE) ALLERG & INFECT DISEASES Corporate Address: JOHNS HOPKINS MED U MD, BALTIMORE (MED)

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 4 (Continued)

The Ten 1976 NIH-Supported Papers
Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	227				21	67	49	52	38	IDENTIFICATION OF MUTAGENIC METABOLITES OF BENZO(A)PYRENE IN MAMMALIAN CELLS. By: HUBERMAN E ; SACHS L ; YANG SK ; GELBOIN V In: PROC NATL ACAD SCI USA 73(2):607-11, FEB 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH FOREIGN
7	216				0	29	68	59	60	1,4-DIAMINOBUTANE (PUTRESCINE), SPERMIDINE, AND SPERMINE. By: TABOR CW ; TABOR H In: ANNU REV BIOCHEM 45:285-306, 1976 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
8	214				0	30	56	62	66	INTRACELLULAR PROTEIN DEGRADATION IN MAMMALIAN AND BACTERIAL CELLS: PART 2. By: GOLDBERG AL ; ST. JOHN AC In: ANNU REV BIOCHEM 45:747-803, 1976 Support source(s): NEUROL DISEASES & STROKE MUSCULAR DYSTROPHY ASSOC Corporate Address: HARVARD MED
9	193				5	25	29	67	67	ASSAY OF PROTEINS IN THE PRESENCE OF INTERFERING MATERIALS. By: BENSADOUN A ; WEINSTEIN D In: ANAL BIOCHEM 70(1):241-50, JAN 76 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: U CAL MED, S DIEGO CORNELL U, ITHACA
10	181				20	52	45	40	24	RECEPTOR-MEDIATED CONTROL OF CHOLESTEROL METABOLISM. By: BROWN MS ; GOLDSTEIN JL In: SCIENCE 191(4223):150-4, 16 JAN 76 Support source(s): HEART,LUNG, & BLOOD INSTITUTE GENERAL MEDICAL SCIENCES AMERICAN HEART ASSOC Corporate Address: U TEX, COMB MED

APPENDIX A

Table 5

The Ten 1977 NIH-Supported Papers Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
1	742					64	175	234	269	A NEW METHOD FOR SEQUENCING DNA. By: MAXAM AM ; GILBERT W In: PROC NATL ACAD SCI USA 74(2):560-4, FEB 77 Support source(s): GENERAL MEDICAL SCIENCES AMERICAN CANCER SOCIETY Corporate Address: HARVARD U, CMBRG
2	432					10	69	169	184	PEPTIDE MAPPING BY LIMITED PROTEOLYSIS IN SODIUM DODECYL SULFATE AND ANALYSIS BY GEL ELECTROPHORESIS. By: CLEVELAND DW ; FISCHER SG ; KIRSCHNER MW ; LAEMMLI UK In: J BIOL CHEM 252(3):1102-6, 10 FEB 77 Support source(s): CANCER INSTITUTE GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION Corporate Address: PRINCETON U
3	296					9	39	104	144	LABELING DEOXYRIBONUCLEIC ACID TO HIGH SPECIFIC ACTIVITY IN VITRO BY NICK TRANSLATION WITH DNA POLYMERASE I. By: RIGBY PW ; DIECKMANN M ; RHODES C ; BERG P In: J MOL BIOL 113(1):237-51, 15 JUN 77 Support source(s): GENERAL MEDICAL SCIENCES AMERICAN CANCER SOCIETY Corporate Address: STANFORD U MED
4	242					16	59	87	80	ANALYSIS OF RESTRICTION FRAGMENTS OF T7 DNA AND DETERMINATION OF MOLECULAR WEIGHTS BY ELECTROPHORESIS IN NEUTRAL AND ALKALINE GELS. By: MCDONELL MW ; SIMON MN ; STUDIER FW In: J MOL BIOL 110(1):119-46, 15 FEB 77 Support source(s): GENERAL MEDICAL SCIENCES Corporate Address: BROOKHVN LABS
5	240					3	47	92	98	FUNCTIONAL ANALYSIS OF TWO HUMAN T-CELL SUBPOPULATIONS: HELP AND SUPPRESSION OF B-CELL RESPONSES BY T CELLS BEARING RECEPTORS FOR IGM OR IGG. By: MORETTA L ; WEBB SR ; GROSSI CE ; LYDYARD PM ; COOPER MD In: J EXP MED 146(1):184-200, 1 JUL 77 Support source(s): CANCER INSTITUTE RESEARCH RESOURCES - NIH Corporate Address: U ALABAMA, BRMGHA U ALAB MED, BRMGH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 5 (Continued)

The Ten 1977 NIH-Supported Papers
Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
5	240					9	62	83	86	COMMON PRECURSOR TO CORTICOTROPINS AND ENDORPHINS. By: MAINS RE ; EIPPER BA ; LING N In: PROC NATL ACAD SCI USA 74(7):3014-8, JUL 77 Support source(s): ARTHR & METABOL DIS RESEARCH RESOURCES - NIH CHILD HEALTH & HUMAN DEV Corporate Address: SALK INST BIOL U COLO MED CTR
7	184					11	62	62	49	MEMBRANE ASYMMETRY. By: ROTHMAN JE ; LENARD J In: SCIENCE 195(4280):743-53, 25 FEB 77 Support source(s): ALLERG & INFECT DISEASES NATL SCIENCE FOUNDATION Corporate Address: MIT, CAMBRIDGE RUTGERS U, N BRUN
8	175					9	47	63	56	A NEW CLASS OF MURINE LEUKEMIA VIRUS ASSOCIATED WITH DEVELOPMENT OF SPONTANEOUS LYMPHOMAS. By: HARILEY JW ; WOLFORD NK ; OLD LJ ; ROWE WP In: PROC NATL ACAD SCI USA 74(2):789-92, FEB 77 Support source(s): CANCER INSTITUTE Corporate Address: SLOAN-KIRG CANC RES INST, NY NIH
9	168					13	69	59	27	SPLICED SEGMENTS AT THE 5' TERMINUS OF ADENOVIRUS 2 LATE MRNA. By: BERGET SM ; MOORE C ; SHARP PA In: PROC NATL ACAD SCI USA 74(8):3171-5, AUG 77 Support source(s): AMERICAN CANCER SOCIETY CANCER INSTITUTE Corporate Address: MIT, CAMBRIDGE
10	167					1	36	61	69	HIGH DENSITY LIPOPROTEIN AS A PROTECTIVE FACTOR AGAINST CORONARY HEART DISEASE. THE FRAMINGHAM STUDY. By: GORDON T ; CASTELLI WP ; HJORTLAND MC ; KANNEL WB ; DAWBER TR In: AM J MED 62(5):707-14, MAY 77 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: NIH

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Table 6

The Ten 1973 NIH Intramural Papers
Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	460	3	24	70	74	78	77	61	73	MICROTUBULE ASSEMBLY IN THE ABSENCE OF ADDED NUCLEOTIDES. By: SHELANSKI ML ; GASKIN F ; CANTOR CR In: PROC NATL ACAD SCI USA 70(3):765-8, MAR 73 Support source(s): HEART,LUNG, & BLOOD INSTITUTE NEUROL DISEASES & STROKE GENERAL MEDICAL SCIENCES Corporate Address: COLUMBIA, NYC NIH
2	245	3	30	33	41	29	45	27	37	EVIDENCE FOR RECYCLING OF SYNAPTIC VESICLE MEMBRANE DURING TRANSMITTER RELEASE AT THE FROG NEUROMUSCULAR JUNCTION. By: HEUSER JE ; REESE TS In: J CELL BIOL 57(2):315-44, MAY 73 Support source(s): NEUROL DISEASES & STROKE Corporate Address: NIH
3	241	1	13	37	37	34	32	44	43	FUNCTION OF MACROPHAGES IN ANTIGEN RECOGNITION BY GUINEA PIG T LYMPHOCYTES. I. REQUIREMENT FOR HISTOCOMPATIBLE MACROPHAGES AND LYMPHOCYTES. By: ROSENTHAL AS ; SHEVACH EM In: J EXP MED 138(5):1194-212, 1 NOV 73 Support source(s): ALLERG & INFECT DISEASES Corporate Address: NIH
4	178	4	23	22	18	21	32	31	27	ASYMMETRIC SEPTAL HYPERTROPHY. ECHOCARDIOGRAPHIC IDENTIFICATION OF THE PATHOGNOMONIC ANATOMIC ABNORMALITY OF IHSS. By: HENRY WL ; CLARK CE ; EPSTEIN SE In: CIRCULATION 47(2):225-33, FEB 73 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: NIH
5	175	7	18	22	30	24	30	28	16	INSULIN-RECEPTOR INTERACTION IN THE OBESE-HYPERGLYCEMIC MOUSE. A MODEL OF INSULIN RESISTANCE. By: KAHN CR ; NEVILLE DM JR ; ROTH J In: J BIOL CHEM 248(1):244-50, 10 JAN 73 Support source(s): NATL INST MENTAL HEALTH ARTHR & METABOL DIS Corporate Address: NIH NIMH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 6 (Continued)

The Ten 1973 NIH Intramural Papers
Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	153	2	15	24	31	21	21	20	19	PEPTIDE HORMONE BINDING TO RECEPTORS: A REVIEW OF DIRECT STUDIES IN VITRO. By: ROTH J In: METABOLISM 22(8):1059-73, AUG 73 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
7	152	1	36	24	21	16	23	22	9	INDEPENDENT SEGREGATION OF LOCI FOR ACTIVATION OF BIOLOGICALLY DISTINGUISHABLE RNA C-TYPE VIRUSES IN MOUSE CELLS. By: AARONSON SA ; STEPHENSON JR In: PROC NATL ACAD SCI USA 70(7):2055-8, JUL 73 Support source(s): CANCER INSTITUTE Corporate Address: NIH
8	151	6	19	22	23	14	17	25	25	CHARACTERISTICS OF THE HUMAN LYMPHOCYTE INSULIN RECEPTOR. By: GAVIN JR 3D ; GORDEN P ; ROTH J ; ARCHER JA ; BUELL DN In: J BIOL CHEM 248(6):2202-7, 25 MAR 73 Support source(s): ARTHR & METABOL DIS CANCER INSTITUTE Corporate Address: NIH
9	145	0	11	10	23	33	22	23	23	FUNCTION OF MACROPHAGES IN ANTIGEN RECOGNITION BY GUINEA PIG T LYMPHOCYTES. II. ROLE OF THE MACROPHAGE IN THE REGULATION OF GENETIC CONTROL OF THE IMMUNE RESPONSE. By: SHEVACH EM ; ROSENTHAL AS In: J EXP MED 138(5):1213-29, 1 NOV 73 Support source(s): ALLERG & INFECT DISEASES Corporate Address: NIH
10	140	0	18	25	31	23	10	21	12	A MOUSE B-CELL ALLOANTIGEN DETERMINED BY GENE(S) LINKED TO THE MAJOR HISTOCOMPATIBILITY COMPLEX. By: SACHS DH ; CONE JL In: J EXP MED 138(6):1289-304, 1 DEC 73 Support source(s): CANCER INSTITUTE Corporate Address: NIH

APPENDIX A

Table 7

The Ten 1974 NIH Intramural Papers Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
1	649		8	30	81	96	125	133	176	A HIGHLY SENSITIVE ADENYLATE CYCLASE ASSAY. By: SALOMON Y ; LONDOS C ; RODBELL M In: ANAL BIOCHEM 58(2):541-8, APR 74 Support source(s): ARTHR & METABOL DIS DENTAL RESEARCH Corporate Address: NIH
2	318		3	42	58	61	53	62	39	ARENE OXIDES: A NEW ASPECT OF DRUG METABOLISM. By: JERINA DM ; DALY JW In: SCIENCE 185(151):573-82, 16 AUG 74 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
3	314		3	28	39	49	67	68	60	INSULIN-DEPENDENT REGULATION OF INSULIN RECEPTOR CONCENTRATIONS: A DIRECT DEMONSTRATION IN CELL CULTURE. By: GAVIN JR 3D ; ROTH J ; NEVILLE DM JR ; MEYTS P DE ; BUELL DN In: PROC NATL ACAD SCI USA 71(1):84-8, JAN 74 Support source(s): ARTHR & METABOL DIS CANCER INSTITUTE FOGARTY INTERNATL CENTER Corporate Address: NIH NIMH
4	214		0	13	34	38	50	41	38	ROLE OF SUPPRESSOR T CELLS IN PATHOGENESIS OF COMMON VARIABLE HYPOGAMMAGLOBULINAEMIA. By: WALDMANN TA ; DURM M ; BRODER S ; BLACKMAN M ; BLAESE RM ; STROBER W In: LANCET 2(7881):609-13, 14 SEP 74 Support source(s): CANCER INSTITUTE Corporate Address: NIH
5	180		12	33	34	33	20	25	23	MODULATION OF INFLAMMATION AND IMMUNITY BY CYCLIC AMP. By: BOURNE HR ; LICHTENSTEIN LM ; MELMON KL ; HENNEY CS ; WEINSTEIN Y SHEARER GM In: SCIENCE 184(132):19-28, 5 APR 74 Support source(s): HEART, LUNG, & BLOOD INSTITUTE GENERAL MEDICAL SCIENCES ALLERG & INFECT DISEASES Corporate Address: U CAL MED, S FRAN JOHNS HOPKINS MED NIH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 7 (Continued)

The Ten 1974 NIH Intramural Papers
Most Highly Cited in 1974-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
		Cites received by citing year								
6	167		5	39	27	28	19	29	28	ADRIAMYCIN. A NEW ANTICANCER DRUG WITH SIGNIFICANT CLINICAL ACTIVITY. By: BLUM RH ; CARTER SK In: ANN INTERN MED 80(2):249-59, FEB 74 Support source(s): CANCER INSTITUTE Corporate Address: NIH
7	165		1	12	21	22	28	37	44	GLUTATHIONE S-TRANSFERASES. THE FIRST ENZYMATIC STEP IN MERCAPTURIC ACID FORMATION. By: HABIG WH ; PABST MJ ; JAKOBY WB In: J BIOL CHEM 249(22):7130-9, 25 NOV 74 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
8	164		0	22	35	25	32	25	25	EVIDENCE OF SUPPRESSOR CELL ACTIVITY IN SPLEENS OF MICE BEARING PRIMARY TUMORS INDUCED BY MOLONEY SARCOMA VIRUS. By: KIRCHNER H ; CHUSED TM ; HERBERMAN RB ; HOLDEN HT ; LAVRIN DH In: J EXP MED 139(6):1473-87, 1 JUN 74 Support source(s): CANCER INSTITUTE DENTAL RESEARCH Corporate Address: NIH UNIDENTIFIED
9	143		2	25	27	13	27	24	25	QUANTITATIVE ASPECTS OF THE INSULIN-RECEPTOR INTERACTION IN LIVER PLASMA MEMBRANES. By: KAHN CR ; FREYCHET P ; ROTH J ; NEVILLE DM JR In: J BIOL CHEM 249(7):2249-57, 10 APR 74 Support source(s): ARTHR & METABOL DIS NATL INST MENTAL HEALTH Corporate Address: NIH NIMH
10	141		1	22	26	42	28	10	12	STUDIES OF THE HUMAN LYMPHOCYTE RECEPTOR FOR HEAT-AGGREGATED OR ANTIGEN-COMPLEXED IMMUNOGLOBULIN. By: DICKLER HB In: J EXP MED 140(2):508-22, 1 AUG 74 Support source(s): CANCER INSTITUTE NATL INSTITUTE OF HEALTH-GENL Corporate Address: NIH

APPENDIX A

Table 8

The Ten 1975 NIH Intramural Papers
Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	189			2	34	35	38	45	35	CLONAL CELLS LINES FROM A FERAL MOUSE EMBRYO WHICH LACK HOST-RANGE RESTRICTIONS FOR MURINE LEUKEMIA VIRUSES. By: HARTLEY JW ; ROWE WP In: VIROLOGY 65(1):128-34, MAY 75 Support source(s): ALLERG & INFECT DISEASES Corporate Address: NIH
2	174			1	26	42	33	41	31	NATURAL CYTOTOXIC REACTIVITY OF MOUSE LYMPHOID CELLS AGAINST SYNGENEIC ACID ALLOGENEIC TUMORS. I. DISTRIBUTION OF REACTIVITY AND SPECIFICITY. By: HERBERMAN RB ; NUNN ME ; LAVRIN DH In: INT J CANCER 16(2):216-29, 15 AUG 75 Support source(s): NATL INSTITUTE OF HEALTH-GENL Corporate Address: NIH UNIDENTIFIED
3	152			1	24	43	28	31	25	ROLE OF CYCLIC NUCLEOTIDES IN GROWTH CONTROL. By: PASTAN IH ; JOHNSON GS ; ANDERSON WB In: ANNU REV BIOCHEM 44:491-522, 1975 Support source(s): CANCER INSTITUTE Corporate Address: NIH
4	144			1	21	43	26	30	23	NATURAL CYTOTOXIC REACTIVITY OF MOUSE LYMPHOID CELLS AGAINST SYNGENEIC AND ALLOGENEIC TUMORS. II. CHARACTERIZATION OF EFFECTOR CELLS. By: HERBERMAN RB ; NUNN ME ; HOLDEN HT ; LAVRIN DH In: INT J CANCER 16(2):230-9, 15 AUG 75 Support source(s): CANCER INSTITUTE Corporate Address: NIH UNIDENTIFIED
5	143			5	25	49	26	22	16	A COMPARISON OF THE DIGESTION OF NUCLEI AND CHROMATIN BY STAPHYLOCOCCAL NUCLEASE. By: SOLLNER-WEBB B ; FELSENFELD G In: BIOCHEMISTRY 14(13):2915-20, JUL 75 Support source(s): ARTHR & METABOL DIS NATL INSTITUTE OF HEALTH-GENL Corporate Address: NIH
6	138			7	18	24	25	42	22	SIMIAN VIRUS 40 FUNCTIONS REQUIRED FOR THE ESTABLISHMENT AND MAINTENANCE OF MALIGNANT TRANSFORMATION. By: MARTIN RG ; CHOU JY In: J VIROL 15(3):599-612, MAR 75 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 8 (Continued)

The Ten 1975 NIH Intramural Papers Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	128			27	35	34	15	9	8	METHYLATED NUCLEOTIDES BLOCK 5'-TERMINUS OF VACCINIA VIRUS MESSENGER RNA. By: WEI CM ; MOSS B In: PROC NATL ACAD SCI USA 72(1):318-22, JAN 75 Support source(s): ALLERG & INFECT DISEASES Corporate Address: NIH
8	123			1	19	28	31	25	19	RAPID CHANGES IN RAT PINEAL BETA-ADRENERGIC RECEPTOR: ALTERATIONS IN L-(3H)ALPRENOLOL BINDING AND ADENYLATE CYCLASE. By: KEBABIAN JW ; ZATZ M ; ROMERO JA ; AXELROD J In: PROC NATL ACAD SCI USA 72(9):3735-9, SEP 75 Support source(s): GENERAL MEDICAL SCIENCES NATL INST MENTAL HEALTH Corporate Address: NIH NIMH
9	112			20	33	24	14	12	9	TYPE C RNA TUMOR VIRUS ISOLATED FROM CULTURED HUMAN ACUTE MYELOGENOUS LEUKEMIA CELLS. By: GALLAGHER RE ; GALLO RC In: SCIENCE 187(4174):350-3, 31 JAN 75 Support source(s): CANCER INSTITUTE Corporate Address: NIH
10	109			14	23	20	22	15	15	INHIBITION OF PROLIFERATION OF LYMPHOMA CELLS AND T LYMPHOCYTES BY SUPPRESSOR CELLS FROM SPLEENS OF TUMOR-BEARING MICE. By: KIRCHNER H ; MUCHMORE AV ; CHUSED TM ; HOLDEN HT ; HERBERMAN RB In: J IMMUNOL 114(1 PT 1):206-10, JAN 75 Support source(s): DENTAL RESEARCH Corporate Address: NIH

APPENDIX A

Table 9

The Ten 1976 NIH Intramural Papers
Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	227				*21	67	49	52	38	IDENTIFICATION OF MUTAGENIC METABOLITES OF BENZO(A)PYRENE IN MAMMALIAN CELLS. By: HUBERMAN E ; SACHS L ; YANG SK ; GELBOIN V In: PROC NATL ACAD SCI USA 73(2):607-11, FEB 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH FOREIGN
2	216				0	29	68	59	60	1,4-DIAMINOBUTANE (PUTRESCINE), SPERMIDINE, AND SPERMINE. By: TABOR CW ; TABOR H In: ANNU REV BIOCHEM 45:285-306, 1976 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
3	165				4	31	53	40	37	CELL SURFACE PROTEIN PARTIALLY RESTORES MORPHOLOGY, ADHESIVENESS, AND CONTACT INHIBITION OF MOVEMENT TO TRANSFORMED FIBROBLASTS. By: YAMADA KM ; YAMADA SS ; PASTAN I In: PROC NATL ACAD SCI USA 73(4):1217-21, APR 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH
4	151				1	45	38	40	27	BENZO(A)PYRENE DIOL EPOXIDES AS INTERMEDIATES IN NUCLEIC ACID BINDING IN VITRO AND IN VIVO. By: WEINSTEIN IB ; JEFFREY AM ; JENNETTE KW ; BLOBSTEIN SH ; HARVEY RG HARRIS C ; AUTRUP H ; KASAI H ; NAKANISHI K In: SCIENCE 193(4253):592-5, 13 AUG 76 Support source(s): CANCER INSTITUTE AMERICAN CANCER SOCIETY Corporate Address: COLUMBIA, NYC COLUMBIA U MED NIH
5	150				5	21	28	41	55	PREVENTION OF CHEMICAL CARCINOGENESIS BY VITAMIN A AND ITS SYNTHETIC ANALOGS (RETINOIDS). By: SPORN MB ; DUNLOP NM ; NEWTON DL ; SMITH JM In: FED PROC 35(6):1332-8, 1 MAY 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 9 (Continued)

The Ten 1976 NIH Intramural Papers
Most Highly Cited in 1976-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
6	149			*	7	24	40	41	37	SERUM LIPOPROTEINS AND CORONARY HEART DISEASE IN A POPULATION STUDY OF HAWAII JAPANESE MEN. By: RHOADS GG ; GULBRANDSEN CL ; KAGAN A In: N ENGL J MED 294(6):293-8, 5 FEB 76 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: NIH
7	148				4	23	35	44	42	AN IMPROVED METHOD FOR ISOLATION OF H-2 AND IA ALLOANTIGENS WITH IMMUNOPRECIPITATION INDUCED BY PROTEIN A-BEARING STAPHYLOCOCCI. By: CULLEN SE ; SCHWARTZ BD In: J IMMUNOL 117(1):136-42, JUL 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH
8	143				7	22	43	32	39	SITE-SITE INTERACTIONS AMONG INSULIN RECEPTORS. CHARACTERIZATION OF THE NEGATIVE COOPERATIVITY. By: DEMEYTS P ; BAINCO AR ; ROTH J In: J BIOL CHEM 241(7):1877-88, 10 APR 76 Support source(s): ARTHR & METABOL DIS FOGARTY INTERNATL CENTER AMERICAN DIABETES ASSOC Corporate Address: NIH
9	140				1	14	45	36	44	MEMBRANE RECEPTORS FOR HORMONES AND NEUROTRANSMITTERS. By: KAHN CR In: J CELL BIOL 70(2 PT 1):261-86, AUG 76 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
10	138				3	18	23	42	52	THE STRUCTURE-ACTIVITY RELATIONS OF SYNTHETIC PEPTIDES AS CHEMOTACTIC FACTORS AND INDUCERS OF LYSOSOMAL SECRETION FOR NEUTROPHILS. By: SHOWELL HJ ; FREER RJ ; ZIGMOND SH ; SCHIFFMANN E ; ASWANIKUMAR S CORCORAN B ; BECKER EL In: J EXP MED 143(5):1154-69, 1 MAY 76 Support source(s): ALLERG & INFECT DISEASES HEART,LUNG, & BLOOD INSTITUTE AMERICAN HEART ASSOC Corporate Address: YALE U MED NIH UNIDENTIFIED

APPENDIX A

Table 10

The Ten 1977 NIH Intramural Papers
Most Highly Cited in 1977-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
1	175					9	47	63	56	A NEW CLASS OF MURINE LEUKEMIA VIRUS ASSOCIATED WITH DEVELOPMENT OF SPONTANEOUS LYMPHOMAS. By: HARTLEY JW ; WOLFORD NK ; OLD LJ ; ROWE WP In: PROC NATL ACAD SCI USA 74(2):789-92, FEB 77 Support source(s): CANCER INSTITUTE Corporate Address: SLOAN-KTRG CANC RES INST, NY NIH
2	167					1	36	61	69	HIGH DENSITY LIPOPROTEIN AS A PROTECTIVE FACTOR AGAINST CORONARY HEART DISEASE. THE FRAMINGHAM STUDY. By: GORDON T ; CASTELLI WP ; HJORTLAND MC ; KANNEL WB ; DAWBER TR In: AM J MED 62(5):707-14, MAY 77 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: NIH
3	124					2	28	49	45	HDL CHOLESTEROL AND OTHER LIPIDS IN CORONARY HEART DISEASE. THE COOPERATIVE LIPOPROTEIN PHENOTYPING STUDY. By: CASTELLI WP ; DOYLE JT ; GORDON T ; HAMES CG ; HJORTLAND MC HULLEY SB ; KAGAN A ; ZUKEL WJ In: CIRCULATION 55(5):767-72, MAY 77 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: INST MED SCI, SF N Y S DEP HLTH, ALB NIH
4	116					3	23	47	43	REAL-TIME RADIONUCLIDE CINEANGIOGRAPHY IN THE NONINVASIVE EVALUATION OF GLOBAL AND REGIONAL LEFT VENTRICULAR FUNCTION AT REST AND DURING EXERCISE IN PATIENTS WITH CORONARY-ARTERY DISEASE. By: BORER JS ; BACHARACH SL ; GREEN MV ; KENT KM ; EPSTEIN SE JOHNSTON GS In: N ENGL J MED 296(15):839-44, 14 APR 77 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: NIH
5	108					0	25	45	38	BIOCHEMICAL EVIDENCE THAT MCF MURINE LEUKEMIA VIRUSES ARE ENVELOPE (ENV) GENE RECOMBINANTS. By: ELDER JH ; GAUTSCH JW ; JENSEN FC ; LERNER RA ; HARTLEY JW ; ROWE WP In: PROC NATL ACAD SCI USA 74(10):4676-80, OCT 77 Support source(s): ALLERG & INFECT DISEASES Corporate Address: SCRIPPS CLINIC NIH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX A

Table 10 (Continued)

The Ten 1977 NIH Intramural Papers
Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	104					13	26	34	31	NATURAL CYTOTOXIC REACTIVITY OF HUMAN LYMPHOCYTES AGAINST A MYELOID CELL LINE: CHARACTERIZATION OF EFFECTOR CELLS. By: WEST WH ; CANNON GB ; KAY HD ; BONNARD GD ; HERBERMAN RB In: J IMMUNOL 118(1):355-61, JAN 77 Support source(s): CANCER INSTITUTE Corporate Address: NIH
7	96					16	38	30	12	BENZO A PYRENE 7,8-DIHYDRODIOL IS MORE CARCINOGENIC THAN BENZO A PYRENE IN NEWBORN MICE. By: KAPITULNIK J ; LEVIN W ; CONNEY AH ; YAGI H ; JERINA DM In: NATURE 266(5600):378-80, 24 MAR 77 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH UNIDENTIFIED
8	92					2	24	33	33	RAPID ANALYSIS OF AMINO ACID PHENYLTHIOHYDANTOINS BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY. By: ZIMMERMAN CL ; APPELLA E ; PISANO JJ In: ANAL BIOCHEM 77(2):569-73, FEB 77 Support source(s): HEART,LUNG, & BLOOD INSTITUTE Corporate Address: NIH
9	90					2	41	35	12	NOVEL MECHANISM FOR RNA MATURATION: THE LEADER SEQUENCES OF SIMIAN VIRUS 40 MRNA ARE NOT TRANSCRIBED ADJACENT TO THE CODING SEQUENCES. By: ALONI Y ; DHAR R ; LAUB O ; HOROWITZ M ; KHOURY G In: PROC NATL ACAD SCI USA 74(9):3686-90, SEP 77 Support source(s): CANCER INSTITUTE Corporate Address: NIH FOREIGN
10	82					2	21	31	28	A FUNCTIONAL COMPARISON OF HUMAN FC-RECEPTOR-BEARING LYMPHOCYTES ACTIVE IN NATURAL CYTOTOXICITY AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY. By: KAY HD ; BONNARD GD ; WEST WH ; HERBERMAN RB In: J IMMUNOL 118(6):2058-66, JUN 77 Support source(s): CANCER INSTITUTE Corporate Address: NIH

APPENDIX B

In Appendix B the 10 BID-MEDLINE papers published each year from 1973 to 1977 that were most highly cited in 1973-80 BID-SCI journals are listed in four categories: (1) U.S.-authored and -supported papers, (2) U.S. papers with non-Federal support, (3) U.S. papers with support unacknowledged, and (4) foreign papers. Papers published in 1978, 1979, and 1980 are not included, as they have fewer than three full years of citations attributed to them (by 1980). The lists include information on rank of citation frequency, the number of citations received annually from 1973 to 1980, a reference to each paper listed, acknowledged support sources, and authors' affiliations.

APPENDIX B

Table 1

The Ten 1973 U.S.-Authored and -Supported Papers Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	821	2	53	104*	112	144	153	140	113	ANALYSIS OF BACTERIOPHAGE T7 EARLY RNAS AND PROTEINS ON SLAB GELS. By: STUDIER FW In: J MOL BIOL 79(2):237-48, 15 SEP 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: BROOKHVN LABS
2	598	0	64	81	95	102	95	94	67	DETECTION OF TWO RESTRICTION ENDONUCLEASE ACTIVITIES IN HAEMOPHILUS PARAINFLUENZAE USING ANALYTICAL AGAROSE--ETHIDIUM BROMIDE ELECTROPHORESIS. By: SHARP PA ; SUGDEN B ; SAMBROOK J In: BIOCHEMISTRY 12(16):3055-63, 31 JUL 73 Support source(s): CANCER INSTITUTE Corporate Address: COLD SP HRBR LAB
3	509	1	18	43	88	92	92	106	69	EFFICIENT TRANSLATION OF TOBACCO MOSAIC VIRUS RNA AND RABBIT GLOBIN 9S RNA IN A CELL-FREE SYSTEM FROM COMMERCIAL WHEAT GERM. By: ROBERTS BE ; PATERSON BM In: PROC NATL ACAD SCI USA 70(8):2330-4, AUG 73 Support source(s): NATL SCIENCE FOUNDATION Corporate Address: FOREIGN
4	460	3	24	70	74	78	77	61	73	MICROTUBULE ASSEMBLY IN THE ABSENCE OF ADDED NUCLEOTIDES. By: SHELANSKI ML ; GASKIN F ; CANTOR CR In: PROC NATL ACAD SCI USA 70(3):765-8, MAR 73 Support source(s): HEART,LUNG, & BLOOD INSTITUTE NEUROL DISEASES & STROKE GENERAL MEDICAL SCIENCES Corporate Address: COLUMBIA, NYC NIH
5	441	0	32	56	80	78	81	65	49	CARCINOGENS ARE MUTAGENS: A SIMPLE TEST SYSTEM COMBINING LIVER HOMOGENATES FOR ACTIVATION AND BACTERIA FOR DETECTION. By: AMES BN ; DURSTON WE ; YAMASAKI E ; LEE FD In: PROC NATL ACAD SCI USA 70(8):2281-5, AUG 73 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) Corporate Address: U CAL, BERKLY
6	412	5	30	46	61	72	64	72	62	FLUOROMETRIC ASSAY OF PROTEINS IN THE NANOGRAM RANGE. By: B OHLEN P ; STEIN S ; DAIRMAN W ; UDENFRIEND S In: ARCH BIOCHEM BIOPHYS 155(1):213-20, MAR 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 1 (Continued)

The Ten 1973 U.S.-Authored and -Supported
Papers Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	396	5	43	42	66	73	62	48	57	CELLULAR LOCALIZATION OF AN EPSTEIN-BARR VIRUS (EBV)-ASSOCIATED COMPLEMENT-FIXING ANTIGEN IN PRODUCER AND NON-PRODUCER LYMPHOBLASTOID CELL LINES. By: REEDMAN BM ; KLEIN G In: INT J CANCER 11(3):499-520, MAY 73 Support source(s): CANCER INSTITUTE Corporate Address: FOREIGN
8	364	14	41	57	52	49	57	51	43	HYPOTHALAMIC POLYPEPTIDE THAT INHIBITS THE SECRETION OF IMMUNOREACTIVE PITUITARY GROWTH HORMONE. By: BRAZEAU P ; VALE W ; BURGUS R ; LING N ; BUTCHER M ; RIVIER J GUILLEMIN R In: SCIENCE 179(68):77-9, 5 JAN 73 Support source(s): PRIVATE NON-PROFIT PRIVATE FOR PROFIT Corporate Address: SALK INST BIOL
9	339	2	49	53	58	53	51	42	31	THE BIOCHEMISTRY OF PLANT LECTINS (PHYTOHEMAGGLUTININS). By: LIS H ; SHARON N In: ANNU REV BIOCHEM 42(0):541-74, 1973 Support source(s): LIBRARY OF MEDICINE NATL INSTITUTE OF HEALTH-GENL DEPT OF AGRICULTURE Corporate Address: FOREIGN
10	331	9	31	47	48	54	52	38	52	OPIATE RECEPTOR: DEMONSTRATION IN NERVOUS TISSUE. By: PERT CB ; SNYDER SH In: SCIENCE 179(77):1011-4, 9 MAR 73 Support source(s): PRIVATE FOR PROFIT Corporate Address: JOHNS HOPKINS MED

APPENDIX B

Table 2

The Ten 1974 U.S.-Authored and -Supported Papers Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	1668		2	22	101	193	313	505	532	A FILM DETECTION METHOD FOR TRITIUM-LABELLED PROTEINS AND NUCLEIC ACIDS IN POLYACRYLAMIDE GELS. By: BONNER WM ; LASKEY RA In: EUR J BIOCHEM 46(1):83-8, 1 JUL 74 Support source(s): PRIVATE NON-PROFIT ARTHRITIS FOUNDATION Corporate Address: FOREIGN
2	649		8	30	81	96	125	133	176	A HIGHLY SENSITIVE ADENYLATE CYCLASE ASSAY. By: SALOMON Y ; LONDOS C ; RODBELL M In: ANAL BIOCHEM 58(2):541-8, APR 74 Support source(s): ARTHR & METABGL DIS DENTAL RESEARCH Corporate Address: NIH
3	466		4	40	89	88	93	87	65	THE ORGANIZATION OF PROTEINS IN THE HUMAN RED BLOOD CELL MEMBRANE. A REVIEW. By: STECK TL In: J CELL BIOL 62(1):1-19, JUL 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CHIC PRITZ MED
4	376		1	42	96	67	61	61	48	THE MOLECULAR ORGANIZATION OF MEMBRANES. By: SINGER SJ In: ANNU REV BIOCHEM 43(0):805-33, 1974 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CAL, SAN DIEGO
5	375		0	11	48	64	79	91	82	A SIMPLIFIED METHOD FOR CYANOGEN BROMIDE ACTIVATION OF AGAROSE FOR AFFINITY CHROMATOGRAPHY. By: MARCH SC ; PARIKH I ; CUATRECASAS P In: ANAL BIOCHEM 60(1):149-52, JUL 74 Support source(s): ARTHR & METABOL DIS GENERAL MEDICAL SCIENCES Corporate Address: JOHNS HOPKINS MED
6	346		5	51	71	98	54	47	20	SPHEROID CHROMATIN UNITS (V BODIES). By: OLINS AL ; OLINS DE In: SCIENCE 183(122):330-2, 25 JAN 74 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) GENERAL MEDICAL SCIENCES Corporate Address: U TENN, KNOXVLL OAK RIDGE LABS

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 2 (Continued)

The Ten 1974 U.S.-Authored and -Supported
Papers Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	344		11	44	63	67	72	48	39	PREDICTION OF PROTEIN CONFORMATION. By: CHOU PY ; FASMAN GD In: BIOCHEMISTRY 13(2):222-45, 15 JAN 74 Support source(s): GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION AMERICAN HEART ASSOC Corporate Address: BRANDEIS U, WALT
8	328		15	39	58	75	50	42	29	FEMALE STEROID HORMONES AND TARGET CELL NUCLEI. By: O'MALLEY BW ; MEANS AR In: SCIENCE 183(125):610-20, 15 FEB 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: BAYLOR U, HOUSTON (MED)
9	318		3	42	58	61	53	62	39	ARENE OXIDES: A NEW ASPECT OF DRUG METABOLISM. By: JERINA DM ; DALY JW In: SCIENCE 185(151):573-82, 16 AUG 74 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
10	314		3	28	39	49	67	68	60	INSULIN-DEPENDENT REGULATION OF INSULIN RECEPTOR CONCENTRATIONS: A DIRECT DEMONSTRATION IN CELL CULTURE. By: GAVIN JR 3D ; ROTH J ; NEVILLE DM JR ; MEYTS P DE ; BUELL DN In: PROC NATL ACAD SCI USA 71(1):84-8, JAN 74 Support source(s): ARTHR & METABOL DIS CANCER INSTITUTE FOGARTY INTERNATL CENTER Corporate Address: NIH NIMH

APPENDIX B

Table 3

The Ten 1975 U.S.-Authored and -Supported Papers Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	1028			3	40	105	178	309	393	HIGH RESOLUTION TWO-DIMENSIONAL ELECTROPHORESIS OF PROTEINS. By: O'FARRELL PH In: J BIOL CHEM 250(10):4007-21, 25 MAY 75 Support source(s): NATL SCIENCE FOUNDATION Corporate Address: U COLO, BOULDER
2	651			0	33	92	141	195	190	METHODS FOR DETECTING CARCINOGENS AND MUTAGENS WITH THE SALMONELLA/MAMMALIAN-MICROSOME MUTAGENICITY TEST. By: AMES BN ; MCCANN J ; YAMASAKI E In: MUTAT RES 31(6):347-64, DEC 75 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) Corporate Address: U CAL, BERKLY
3	554			0	9	34	93	201	217	RAPID ISOLATION OF ANTIGENS FROM CELLS WITH A STAPHYLOCOCCAL PROTEIN A-ANTIBODY ADSORBENT: PARAMETERS OF THE INTERACTION OF ANTIBODY-ANTIGEN COMPLEXES WITH PROTEIN A. By: KESSLER SW In: J IMMUNOL 115(6):1617-24, DEC 75 Support source(s): CANCER INSTITUTE Corporate Address: UCLA MED SCH
4	535			0	91	132	121	101	90	IDENTIFICATION OF TWO RELATED PENTAPEPTIDES FROM THE BRAIN WITH POTENT OPIATE AGONIST ACTIVITY. By: HUGHES J ; SMITH TW ; KOSTERLITZ HW ; FOTHERGILL LA ; MORGAN BA MORRIS HR In: NATURE 258(5536):577-80, 18 DEC 75 Support source(s): NATL INST DRUG ABUSE (NIDA) FOREIGN GOVERNMENT Corporate Address: FOREIGN
5	521			0	40	101	116	154	110	DETECTION OF CARCINOGENS AS MUTAGENS IN THE SALMONELLA/MICROSOME TEST: ASSAY OF 300 CHEMICALS. By: MCCANN J ; CHOI E ; YAMASAKI E ; AMES BN In: PROC NATL ACAD SCI USA 72(12):5135-9, DEC 75 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) AMERICAN CANCER SOCIETY Corporate Address: U CAL, BERKLY

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 3 (Continued)

The Ten 1975 U.S.-Authored and -Supported Papers Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	475			2	14	76	103	151	129	TRANSFER OF PROTEINS ACROSS MEMBRANES. I. PRESENCE OF PROTEOLYTICALLY PROCESSED AND UNPROCESSED NASCENT IMMUNOGLOBULIN LIGHT CHAINS ON MEMBRANE-BOUND RIBOSOMES OF MURINE MYELOMA. By: BLOBEL G ; DOBBERSTEIN B In: J CELL BIOL 67(3):835-51, DEC 75 Support source(s): CANCER INSTITUTE Corporate Address: ROCKFLR U, NY
7	333			5	60	72	62	66	68	FUNCTIONAL SUBCLASSES OF T-LYMPHOCYTES BEARING DIFFERENT LY ANTIGENS. I. THE GENERATION OF FUNCTIONALLY DISTINCT T-CELL SUBCLASSES IS A DIFFERENTIATIVE PROCESS INDEPENDENT OF ANTIGEN. By: CANTOR H ; BOYSE EA In: J EXP MED 141(6):1376-89, 1 JUN 75 Support source(s): CANCER INSTITUTE ALLERG & INFECT DISEASES Corporate Address: CHILDRENS CANC RES FDN SLOAN-KTRG CANC RES INST, NY
8	312			4	33	49	65	80	81	INTRACELLULAR ASPECTS OF THE PROCESS OF PROTEIN SYNTHESIS. By: PALADE G In: SCIENCE 189(4200):347-58, 1 AUG 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: YALE U MED
9	303			1	36	70	53	86	57	PROTEIN PHOSPHORYLATION. By: RUBIN CS ; ROSEN OM In: ANNU REV BIOCHEM 44:831-87, 1975 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: ALB EINST, YESHIVA
10	295			2	23	39	55	77	99	NUCLEOTIDE SEQUENCE OF THE RIGHTWARD OPERATOR OF PHAGE LAMBDA. By: MANIATIS T ; JEFFREY A ; KLEID DG In: PROC NATL ACAD SCI USA 72(3):1184-8, MAR 75 Support source(s): NATL SCIENCE FOUNDATION NATL INSTITUTE OF HEALTH-GENL Corporate Address: HARVARD U, CMBRG

APPENDIX B

Table 4

The Ten 1976 U.S.-Authored and -Supported Papers Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	1077				* 0	30	140	360	547	A RAPID AND SENSITIVE METHOD FOR THE QUANTITATION OF MICROGRAM QUANTITIES OF PROTEIN UTILIZING THE PRINCIPLE OF PROTEIN-DYE BINDING. By: BRADFORD MM In: ANAL BIOCHEM 72:248-54, 7 MAY 76 Support source(s): CHILD HEALTH & HUMAN DEV FORD FOUNDATION Corporate Address: U GA, ATHENS
2	280				22	62	74	65	57	SURFACE MODULATION IN CELL RECOGNITION AND CELL GROWTH. By: EDELMAN GM In: SCIENCE 192(4236):218-26, 16 APR 76 Support source(s): ALLERG & INFECT DISEASES ARTHR & METABOL DIS CHILD HEALTH & HUMAN DEV Corporate Address: ROCKFLR U, NY
3	253				3	41	70	71	68	CELL SURFACE PROTEINS AND MALIGNANT TRANSFORMATION. By: HYNES RO In: BIOCHIM BIOPHYS ACTA 458(1):73-107, 30 APR 76 Support source(s): CANCER INSTITUTE Corporate Address: MIT, CAMBRIDGE
4	250				16	49	72	60	53	TRANSMEMBRANE CONTROL OF THE RECEPTORS ON NORMAL AND TUMOR CELLS. I. CYTOPLASMIC INFLUENCE OVER SURFACE COMPONENTS. By: NICOLSON GL In: BIOCHIM BIOPHYS ACTA 457(1):57-108. 13 APR 76 Support source(s): CANCER BIOL & DIAG - CANC INST NATL SCIENCE FOUNDATION CANCER INSTITUTE Corporate Address: U CAL, IRVINE SALK INST BIOL
5	236				4	43	58	74	57	THE ROLE OF POLYPRENOL-LINKED SUGARS IN GLYCOPROTEIN SYNTHESIS. By: WAECHTER CJ ; LENNARZ WJ In: ANNU REV BIOCHEM 45:95-112, 1976 Support source(s): NEUROL DISEASES & STROKE UNIV+MED SCHOOLS(STATE) ALLERG & INFECT DISEASES Corporate Address: JOHNS HOPKINS MED U MD, BALTIMORE (MED)

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B
Table 4 (Continued)

The Ten 1976 U.S.-Authored and -Supported Papers Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	229				1	58	46	60	64	CHROMOSOMAL SUBUNITS IN ACTIVE GENES HAVE AN ALTERED CONFORMATION. By: WEINTRAUB H ; GROUDINE M In: SCIENCE 193(4256):848-56, 3 SEP 76 Support source(s): NATL SCIENCE FOUNDATION AMERICAN CANCER SOCIETY Corporate Address: PRINCETON U
7	227				21	67	49	52	38	IDENTIFICATION OF MUTAGENIC METABOLITES OF BENZO(A)PYRENE IN MAMMALIAN CELLS. By: HUBERMAN E ; SACHS L ; YANG SK ; GELBOIN V In: PROC NATL ACAD SCI USA 73(2):607-11, FEB 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH FOREIGN
8	216				0	29	68	59	60	1,4-DIAMINOBUTANE (PUTRESCINE), SPERMIDINE, AND SPERMINE. By: TABOR CW ; TABOR H In: ANNU REV BIOCHEM 45:285-306, 1976 Support source(s): ARTHR & METABOL DIS Corporate Address: NIH
9	214				0	30	56	62	66	INTRACELLULAR PROTEIN DEGRADATION IN MAMMALIAN AND BACTERIAL CELLS: PART 2. By: GOLDBERG AL ; ST. JOHN AC In: ANNU REV BIOCHEM 45:747-803, 1976 Support source(s): NEUROL DISEASES & STROKE MUSCULAR DYSTROPHY ASSOC Corporate Address: HARVARD MED
10	212				2	19	46	93	52	COMPARATIVE ASPECTS OF GLYCOPROTEIN STRUCTURE. By: KORNFELD R ; KORNFELD S In: ANNU REV BIOCHEM 45:217-37, 1976 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: WASHINGTON U MED

APPENDIX B

Table 5

The Ten 1977 U.S.-Authored and -Supported Papers Most Highly Cited in 1977-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
1	742					64	175	234	269	A NEW METHOD FOR SEQUENCING DNA. By: MAXAM AM ; GILBERT W In: PROC NATL ACAD SCI USA 74(2):560-4, FEB 77 Support source(s): GENERAL MEDICAL SCIENCES AMERICAN CANCER SOCIETY Corporate Address: HARVARD U, CMBRG
2	432					10	69	169	184	PEPTIDE MAPPING BY LIMITED PROTEOLYSIS IN SODIUM DODECYL SULFATE AND ANALYSIS BY GEL ELECTROPHORESIS. By: CLEVELAND DW ; FISCHER SG ; KIRSCHNER MW ; LAEMMLI UK In: J BIOL CHEM 252(3):1102-6, 10 FEB 77 Support source(s): CANCER INSTITUTE GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION Corporate Address: PRINCETON U
3	296					9	39	104	144	LABELING DEOXYRIBONUCLEIC ACID TO HIGH SPECIFIC ACTIVITY IN VITRO BY NICK TRANSLATION WITH DNA POLYMERASE I. By: RIGBY PW ; DIECKMANN M ; RHODES C ; BERG P In: J MOL BIOL 113(1):237-51, 15 JUN 77 Support source(s): GENERAL MEDICAL SCIENCES AMERICAN CANCER SOCIETY Corporate Address: STANFORD U MED
4	242					16	59	87	80	ANALYSIS OF RESTRICTION FRAGMENTS OF T7 DNA AND DETERMINATION OF MOLECULAR WEIGHTS BY ELECTROPHORESIS IN NEUTRAL AND ALKALINE GELS. By: MCDONELL MW ; SIMON MN ; STUDIER FW In: J MOL BIOL 110(1):119-46, 15 FEB 77 Support source(s): GENERAL MEDICAL SCIENCES Corporate Address: BROOKHVN LABS
5	240					3	47	92	98	FUNCTIONAL ANALYSIS OF TWO HUMAN T-CELL SUBPOPULATIONS: HELP AND SUPPRESSION OF B-CELL RESPONSES BY T CELLS BEARING RECEPTORS FOR IGM OR IGG. By: MORETTA L ; WEBB SR ; GROSSI CE ; LYDYARD PM ; COOPER MD In: J EXP MED 146(1):184-200, 1 JUL 77 Support source(s): CANCER INSTITUTE RESEARCH RESOURCES - NIH Corporate Address: U ALABAMA, BRMGHA U ALAB MED, BRMGH

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 5 (Continued)

The Ten 1977 U.S.-Authored and -Supported Papers Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
5	240					9	62	83	86	COMMON PRECURSOR TO CORTICOTROPINS AND ENDORPHINS. By: MAINS RE ; EIPPER BA ; LING N In: PROC NATL ACAD SCI USA 74(7):3014-8, JUL 77 Support source(s): ARTHR & METABOL DIS RESEARCH RESOURCES - NIH CHILD HEALTH & HUMAN DEV Corporate Address: SALK INST BIOL U COLO MED CTR
7	228					12	49	80	87	STRUCTURE OF CHROMATIN. By: KORNBERG RD In: ANNU REV BIOCHEM 46:931-54, 1977 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: HARVARD MED
8	184					11	62	62	49	MEMBRANE ASYMMETRY. By: ROTHMAN JE ; LENARD J In: SCIENCE 195(4280):743-53, 25 FEB 77 Support source(s): ALLERG & INFECT DISEASES NATL SCIENCE FOUNDATION Corporate Address: MIT, CAMBRIDGE RUTGERS U, N BRUN
9	181					6	29	79	67	THE LOW-DENSITY LIPOPROTEIN PATHWAY AND ITS RELATION TO ATHEROSCLEROSIS. By: GOLDSTEIN JL ; BROWN MS In: ANNU REV BIOCHEM 46:897-930, 1977 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U TEX, COMB MED
10	175					9	47	63	56	A NEW CLASS OF MURINE LEUKEMIA VIRUS ASSOCIATED WITH DEVELOPMENT OF SPONTANEOUS LYMPHOMAS. By: HARTLEY JW ; WOLFORD NK ; OLD LJ ; ROWE WP In: PROC NATL ACAD SCI USA 74(2):789-92, FEB 77 Support source(s): CANCER INSTITUTE Corporate Address: SLOAN-KTRG CANC RES INST, NY NIH

APPENDIX B

Table 6

The Ten 1973 U.S. Papers with Non-Federal Support Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	364	14	41	57	52	49	57	51	43	HYPOTHALAMIC POLYPEPTIDE THAT INHIBITS THE SECRETION OF IMMUNOREACTIVE PITUITARY GROWTH HORMONE. By: BRAZEAU P ; VALE W ; BURGUS R ; LING N ; BUTCHER M ; RIVIER J GUILLEMIN R In: SCIENCE 179(68):77-9, 5 JAN 73 Support source(s): PRIVATE NON-PROFIT PRIVATE FOR PROFIT Corporate Address: SALK INST BIOL
2	331	9	31	47	48	54	52	38	52	OPIATE RECEPTOR: DEMONSTRATION IN NERVOUS TISSUE. By: PERT CB ; SNYDER SH In: SCIENCE 179(77):1011-4, 9 MAR 73 Support source(s): PRIVATE FOR PROFIT Corporate Address: JOHNS HOPKINS MED
3	263	3	20	23	33	43	49	47	45	A HOMOLOGOUS RADIOIMMUNOASSAY FOR HUMAN PROLACTIN. By: SINHA YN ; SELBY FW ; LEWIS UJ ; VANDERLAAN WP In: J CLIN ENDOCRINOL METAB 36(3):509-16, MAR 73 Support source(s): ARTHR & METABOL DIS AMERICAN CANCER SOCIETY Corporate Address: SCRIPPS CLINIC
4	246	5	23	23	35	43	40	31	46	AN ENZYMATIC FUNCTION ASSOCIATED WITH TRANSFORMATION OF FIBROBLASTS BY ONCOGENIC VIRUSES. I. CHICK EMBRYO FIBROBLAST CULTURES TRANSFORMED BY AVIAN RNA TUMOR VIRUSES. By: UNKELESS JC ; TOBIA A ; OSSOWSKI L ; QUIGLEY JP ; RIFKIN DB REICH E In: J EXP MED 137(1):85-111, 1 JAN 73 Support source(s): AMERICAN CANCER SOCIETY CANCER INSTITUTE Corporate Address: ROCKFLR U, NY
5	221	11	48	41	35	36	21	16	13	COMBINED STUDIES OF COMPLEMENT RECEPTOR AND SURFACE IMMUNOGLOBULIN-BEARING CELLS AND SHEEP ERYTHROCYTE ROSETTE-FORMING CELLS IN NORMAL AND LEUKEMIC HUMAN LYMPHOCYTES. By: ROSS GD ; RABELLINO EM ; POLLEY MJ ; GREY HM In: J CLIN INVEST 52(2):377-85, FEB 73 Support source(s): ALLERG & INFECT DISEASES AMERICAN HEART ASSOC Corporate Address: SCRIPPS CLINIC NIL JWSH HP, DNVR

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 6 (Continued)

The Ten 1973 U.S. Papers with Non-Federal Support Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	217	1	34	39	40	38	29	17	19	LATERAL PHASE SEPARATIONS IN MEMBRANE LIPIDS AND THE MECHANISM OF SUGAR TRANSPORT IN ESCHERICHIA COLI. By: LINDEN CD ; WRIGHT KL ; MCCONNELL HM ; FOX CF In: PROC NATL ACAD SCI USA 70(8):2271-5, AUG 73 Support source(s): GENERAL MEDICAL SCIENCES ALLERG & INFECT DISEASES AMERICAN CANCER SOCIETY Corporate Address: UCLA STANFORD U
7	209	1	19	28	45	40	24	30	22	THYMUS-DERIVED ROSETTE-FORMING CELLS IN VARIOUS HUMAN DISEASE STATES: CANCER, LYMPHOMA, BACTERIAL AND VIRAL INFECTIONS, AND OTHER DISEASES. By: WYBRAN J ; FUDENBERG HH In: J CLIN INVEST 52(5):1026-32, MAY 73 Support source(s): CHILD HEALTH & HUMAN DEV PRIVATE FOR PROFIT AMERICAN CANCER SOCIETY Corporate Address: U CAL MED, S FRAN MT ZION MED CTR
8	208	3	12	34	40	31	28	24	36	STEREOSPECIFIC BINDING OF THE POTENT NARCOTIC ANALGESIC (3H) ETORPHINE TO RAT-BRAIN HOMOGENATE. By: SIMON EJ ; HILLER JM ; EDELMAN I In: PROC NATL ACAD SCI USA 70(7):1947-9, JUL 73 Support source(s): DEPT OF AGRICULTURE PRIVATE FOR PROFIT Corporate Address: NYU MED
9	206	3	20	30	34	43	27	24	25	AN IMPROVED SCINTILLATION COCKTAIL OF HIGH-SOLUBILIZING POWER. By: ANDERSON LE ; MCCLURE WO In: ANAL BIOCHEM 51(1):173-9, JAN 73 Support source(s): NEUROL DISEASES & STROKE OTHER FEDERAL GOVERNMENT PRIVATE FOR PROFIT Corporate Address: U ILL, URBANA
10	193	0	12	18	24	25	29	51	34	EXTERNAL LABELING OF CELL SURFACE GALACTOSE AND GALACTOSAMINE IN GLYCOLIPID AND GLYCOPROTEIN OF HUMAN ERYTHROCYTES. By: GAHMBERG CT ; HAKOMORI SI In: J BIOL CHEM 248(12):4311-7, 25 JUN 73 Support source(s): CANCER INSTITUTE AMERICAN CANCER SOCIETY FOGARTY INTERNATL CENTER Corporate Address: U WASH MED

APPENDIX B

Table 7

The Ten 1974 U.S. Papers with Non-Federal Support Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	1668		2	22	101	193	313	505	532	A FILM DETECTION METHOD FOR TRITIUM-LABELLED PROTEINS AND NUCLEIC ACIDS IN POLYACRYLAMIDE GELS. By: BONNER WM ; LASKEY RA In: EUR J BIOCHEM 46(1):83-8, 1 JUL 74 Support source(s): PRIVATE NON-PROFIT ARTHRITIS FOUNDATION Corporate Address: FOREIGN
2	344		11	44	63	67	72	48	39	PREDICTION OF PROTEIN CONFORMATION. By: CHOU PY ; FASMAN GD In: BIOCHEMISTRY 13(2):222-45, 15 JAN 74 Support source(s): GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION AMERICAN HEART ASSOC Corporate Address: BRANDEIS U, WALT
3	245		8	10	20	31	48	63	65	MUSCARINIC CHOLINERGIC BINDING IN RAT BRAIN. By: YAMAMURA HI ; SNYDER SH In: PROC NATL ACAD SCI USA 71(5):1725-9, MAY 74 Support source(s): NATL INST MENTAL HEALTH JOHN HARTFORD FOUNDATION Corporate Address: JOHNS HOPKINS MED
4	237		1	35	58	36	41	38	28	MEMBRANE RECEPTORS. By: CUATRECASAS P In: ANNU REV BIOCHEM 43(0):169-214, 1974 Support source(s): ARTHR & METABOL DIS NATL SCIENCE FOUNDATION AMERICAN CANCER SOCIETY Corporate Address: JOHNS HOPKINS MED
5	228		6	45	55	62	21	27	12	CHROMATIN STRUCTURE; OLIGOMERS OF THE HISTONES. By: KORNBERG RD ; THOMAS JO In: SCIENCE 184(139):865-8, 24 MAY 74 Support source(s): PRIVATE NON-PROFIT Corporate Address: FOREIGN

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 7 (Continued)

The Ten 1974 U.S. Papers with Non-Federal Support Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	227		0	6	31	39	43	53	55	MAGNESIUM PRECIPITATION OF RIBONUCLEOPROTEIN COMPLEXES. EXPEDIENT TECHNIQUES FOR THE ISOLATION OF UNDERGRADED POLYSOMES AND MESSENGER RIBONUCLEIC ACID. By: PALMITER RD In: BIOCHEMISTRY 13(17):3606-15, 13 AUG 74 Support source(s): CHILD HEALTH & HUMAN DEV NATL SCIENCE FOUNDATION PRIVATE FOR PROFIT Corporate Address: HARVARD U, CMBRG
6	227		14	31	43	44	29	31	35	CONFORMATIONAL PARAMETERS FOR AMINO ACIDS IN HELICAL, BETA-SHEET, AND RANDOM COIL REGIONS CALCULATED FROM PROTEINS. By: CHOU PY ; FASMAN GD In: BIOCHEMISTRY 13(2):211-22, 15 JAN 74 Support source(s): GENERAL MEDICAL SCIENCES NATL SCIENCE FOUNDATION AMERICAN HEART ASSOC Corporate Address: BRANDEIS U, WALT
8	222		12	51	47	40	31	22	19	NONHISTONE CHROMOSOMAL PROTEINS AND GENE REGULATION. By: STEIN GS ; SPELSBERG TC ; KLEINSMITH LJ In: SCIENCE 183(127):817-24, 1 MAR 74 Support source(s): CANCER INSTITUTE NATL SCIENCE FOUNDATION AMERICAN CANCER SOCIETY Corporate Address: U FLA MED U MICH, ANN ARBR MAYO FDN, ROCH
9	208		2	21	32	30	33	53	37	BINDING AND DEGRADATION OF LOW DENSITY LIPOPROTEINS BY CULTURED HUMAN FIBROBLASTS. COMPARISON OF CELLS FROM A NORMAL SUBJECT AND FROM A PATIENT WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA. By: GOLDSTEIN JL ; BROWN MS In: J BIOL CHEM 249(16):5153-62, 25 AUG 74 Support source(s): AMERICAN HEART ASSOC GENERAL MEDICAL SCIENCES HEART, LUNG, & BLOOD INSTITUTE Corporate Address: U TEX, COMB MED

APPENDIX B

Table 7 (Continued)

The Ten 1974 U.S. Papers with Non-Federal Support Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
9	288		3	32	51	39	36	28	19	DOPAMINE-SENSITIVE ADENYLATE CYCLASE IN MAMMALIAN BRAIN: A POSSIBLE SITE OF ACTION OF ANTIPSYCHOTIC DRUGS. By: CLEMENT-CORMIER YC ; KEBABIAN JW ; PETZOLD GL ; GREENGARD P In: PROC NATL ACAD SCI USA 71(4):1113-7, APR 74 Support source(s): NEUROL DISEASES & STROKE NATL INST MENTAL HEALTH PRIVATE NON-PROFIT Corporate Address: YALE U MED

APPENDIX B

Table 8

The Ten 1975 U.S. Papers with Non-Federal Support Most Highly Cited in 1975-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
		Cites received by citing year								
1	521			0	40	101	116	154	110	DETECTION OF CARCINOGENS AS MUTAGENS IN THE SALMONELLA/MICROSOME TEST: ASSAY OF 300 CHEMICALS. By: MCCANN J ; CHOI E ; YAMASAKI E ; AMES BN In: PROC NATL ACAD SCI USA 72(12):5135-9, DEC 75 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) AMERICAN CANCER SOCIETY Corporate Address: U CAL, BERKLY
2	246			12	31	49	55	56	43	STUDIES ON THE CLEAVAGE OF BACTERIOPHAGE LAMBDA DNA WITH ECORI RESTRICTION ENDONUCLEASE. By: THOMAS M ; DAVIS RW In: J MOL BIOL 91(3):315-28, 25 JAN 75 Support source(s): GENERAL MEDICAL SCIENCES PRIVATE FOR PROFIT Corporate Address: STANFORD U MED
3	230			10	42	52	51	40	35	DETECTION OF CARCINOGENS AS MUTAGENS: BACTERIAL TESTER STRAINS WITH R FACTOR PLASMIDS. By: MCCANN J ; SPINGARN NE ; KOBORI J ; AMES BN In: PROC NATL ACAD SCI USA 72(3):979-83, MAR 75 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) AMERICAN CANCER SOCIETY Corporate Address: U CAL, BERKLY
4	214			1	27	46	39	52	49	THE SODIUM-POTASSIUM ADENOSINE TRIPHOSPHATASE: PHARMACOLOGICAL, PHYSIOLOGICAL AND BIOCHEMICAL ASPECTS. By: SCHWARTZ A ; LINDENMAYER GE ; ALLEN JC In: PHARMACOL REV 27(01):3-134, MAR 75 Support source(s): HEART,LUNG, & BLOOD INSTITUTE NATL INSTITUTE OF HEALTH-GENL AMERICAN HEART ASSOC Corporate Address: BAYLOR U, HOUSTON (MED) UNIDENTIFIED
5	203			3	51	37	36	49	27	BONE-MARROW TRANSPLANTATION (FIRST OF TWO PARTS). By: THOMAS E ; STORB R ; CLIFT RA ; FEFER A ; JOHNSON FL ; NEIMAN PE LERNER KG ; GLUCKSBERG H ; BUCKNER CD In: N ENGL J MED 292(16):832-43, 17 APR 75 Support source(s): CANCER INSTITUTE ALLERG & INFECT DISEASES AMERICAN CANCER SOCIETY Corporate Address: U WASH MED UNIDENTIFIED

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 8 (Continued)

The Ten 1975 U.S. Papers with Non-Federal Support Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	170			4	24	35	45	32	30	CATECHOLAMINE-INDUCED SUBSENSITIVITY OF ADENYLATE CYCLASE ASSOCIATED WITH LOSS OF BETA-ADRENERGIC RECEPTOR BINDING SITES. By: MUKHERJEE C ; CARON MG ; LEFKOWITZ RJ In: PROC NATL ACAD SCI USA 72(5):1945-9, MAY 75 Support source(s): HEART,LUNG, & BLOOD INSTITUTE AMERICAN HEART ASSOC Corporate Address: DUKE MED
7	161			2	13	39	28	50	29	REGULATION OF TUMOR ANTIGEN SYNTHESIS BY SIMAIN VIRUS 40 GENE A. By: TEGTMEYER P ; SCHWARTZ M ; COLLINS JK ; RUNDELL K In: J VIROL 16(1):168-78, JUL 75 Support source(s): AMERICAN CANCER SOCIETY PRIVATE NON-PROFIT CANCER INSTITUTE Corporate Address: CASE-WSTRN U. CLE
8	149			0	30	44	34	20	21	IN VITRO CELL-MEDIATED IMMUNE RESPONSES TO THE MALE SPECIFIC(H-Y) ANTIGEN IN MICE. By: GORDON RD ; SIMPSON E ; SAMELSON LE In: J EXP MED 142(5):1108-20, 1 NOV 75 Support source(s): GENERAL MEDICAL SCIENCES UNIV+MED SCHOOLS(STATE) Corporate Address: FOREIGN
9	145			0	21	40	33	26	25	CONTROL OF GROWTH OF MAMMALIAN CELLS IN CELL CULTURE. By: HOLLEY RW In: NATURE 258(5535):487-90, 11 DEC 75 Support source(s): AMERICAN CANCER SOCIETY CANCER INSTITUTE NATL SCIENCE FOUNDATION Corporate Address: SALK INST BIOL
10	143			1	9	18	39	37	39	PROPERTIES OF GAMMA-AMINOBUTYRIC ACID (GABA) RECEPTOR BINDING IN RAT BRAIN SYNAPTIC MEMBRANE FRACTIONS. By: ENNA SJ ; SNYDER SH In: BRAIN RES 100(1):81-97, 12 DEC 75 Support source(s): NATL INST MENTAL HEALTH JOHN HARTFORD FOUNDATION Corporate Address: JOHNS HOPKINS MED

APPENDIX B

Table 9

The Ten 1976 U.S. Papers with Non-Federal Support Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
1	1077				0	30	140	360	547	A RAPID AND SENSITIVE METHOD FOR THE QUANTITATION OF MICROGRAM QUANTITIES OF PROTEIN UTILIZING THE PRINCIPLE OF PROTEIN-DYE BINDING. By: BRADFORD MM In: ANAL BIOCHEM 72:248-54, 7 MAY 76 Support source(s): CHILD HEALTH & HUMAN DEV FORD FOUNDATION Corporate Address: U GA, ATHENS
2	236				4	43	58	74	57	THE ROLE OF POLYPRENOL-LINKED SUGARS IN GLYCOPROTEIN SYNTHESIS. By: WAECHTER CJ ; LENNARZ WJ In: ANNU REV BIOCHEM 45:95-112, 1976 Support source(s): NEUROL DISEASES & STROKE UNIV+MED SCHOOLS(STATE) ALLERG & INFECT DISEASES Corporate Address: JOHNS HOPKINS MED U MD, BALTIMORE (MED)
3	229				1	58	46	60	64	CHROMOSOMAL SUBUNITS IN ACTIVE GENES HAVE AN ALTERED CONFORMATION. By: WEINTRAUB H ; GROUDINE M In: SCIENCE 193(4256):848-56, 3 SEP 76 Support source(s): NATL SCIENCE FOUNDATION AMERICAN CANCER SOCIETY Corporate Address: PRINCETON U
4	214				0	30	56	62	66	INTRACELLULAR PROTEIN DEGRADATION IN MAMMALIAN AND BACTERIAL CELLS: PART 2. By: GOLDBERG AL ; ST. JOHN AC In: ANNU REV BIOCHEM 45:747-803, 1976 Support source(s): NEUROL DISEASES & STROKE MUSCULAR DYSTROPHY ASSOC Corporate Address: HARVARD MED
5	181				20	52	45	40	24	RECEPTOR-MEDIATED CONTROL OF CHOLESTEROL METABOLISM. By: BROWN MS ; GOLDSTEIN JL In: SCIENCE 191(4223):150-4, 16 JAN 76 Support source(s): HEART,LUNG, & BLOOD INSTITUTE GENERAL MEDICAL SCIENCES AMERICAN HEART ASSOC Corporate Address: U TEX, COMB MED

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 9 (Continued)

The Ten 1976 U.S. Papers with Non-Federal Support Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	188				*14	51	46	36	33	ISOLATION AND STRUCTURE OF AN UNTRIAKONTAPEPTIDE WITH OPIATE ACTIVITY FROM CAMEL PITUITARY GLANDS. By: LI CH ; CHUNG D In: PROC NATL ACAD SCI USA 73(4):1145-8, APR 76 Support source(s): PRIVATE NON-PROFIT Corporate Address: U CAL MED, S FRAN
7	170				4	13	27	61	65	METHYLMERCURY AS A REVERSIBLE DENATURING AGENT FOR AGAROSE GEL ELECTROPHORESIS. By: BAILEY JM ; DAVIDSON N In: ANAL BIOCHEM 70(1):75-85, JAN 76 Support source(s): CANCER INSTITUTE PRIVATE NON-PROFIT Corporate Address: CALTECH, PASADENA
8	156				1	12	39	46	58	EFFICEINT TRANSCRIPTION OF RNA INTO DNA BY AVIAN SARCOMA VIRUS POLYMERASE. By: TAYLOR JM ; ILLMENSEE R ; SUMMERS J In: BIOCHIM BIOPHYS ACTA 442(3):324-30, 6SEP 76 Support source(s): CANCER INSTITUTE RESEARCH RESOURCES - NIH STATE,LOCAL,REG GOVT Corporate Address: INST CNCR RES, PHL
9	151				1	45	38	40	27	BENZO(A)PYRENE DIOL EPOXIDES AS INTERMEDIATES IN NUCLEIC ACID BINDING IN VITRO AND IN VIVO. By: WEINSTEIN IB ; JEFFREY AM ; JENNETTE KW ; BLOBSTEIN SH ; HARVEY RG HARRIS C ; AUTRUP H ; KASAI H ; NAKANISHI K In: SCIENCE 193(4253):592-5, 13 AUG 76 Support source(s): CANCER INSTITUTE AMERICAN CANCER SOCIETY Corporate Address: COLUMBIA, NYC COLUMBIA U MED NIH
10	148				3	26	37	42	40	DISTRIBUTION OF IA-LIKE MOLECULES ON THE SURFACE OF NORMAL AND LEUKEMIC HUMAN CELLS. By: SCHLOSSMAN SF ; CHESS L ; HUMPHREYS RE ; STROMINGER JL In: PROC NATL ACAD SCI USA 73(4):1288-92, APR 76 Support source(s): ALLERG & INFECT DISEASES CANCER INSTITUTE PRIVATE NON-PROFIT Corporate Address: HARVARD MED HARVARD U, CMBRG

APPENDIX B

Table 10

The Ten 1977 U.S. Papers with Non-Federal Support Most Highly Cited in 1977-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
1	742					64	175	234	269	A NEW METHOD FOR SEQUENCING DNA. By: MAXAM AM ; GILBERT W In: PROC NATL ACAD SCI USA 74(2):560-4, FEB 77 Support source(s): GENERAL MEDICAL SCIENCES AMERICAN CANCER SOCIETY Corporate Address: HARVARD U, CMBRG
2	296					9	39	104	144	LABELING DEOXYRIBONUCLEIC ACID TO HIGH SPECIFIC ACTIVITY IN VITRO BY NICK TRANSLATION WITH DNA POLYMERASE I. By: RIGBY PW ; DIECKMANN M ; RHODES C ; BERG P In: J MOL BIOL 113(1):237-51, 15 JUN 77 Support source(s): GENERAL MEDICAL SCIENCES AMERICAN CANCER SOCIETY Corporate Address: STANFORD U MED
3	168					13	69	59	27	SPLICED SEGMENTS AT THE 5' TERMINUS OF ADENOVIRUS 2 LATE MRNA. By: BERGET SM ; MOORE C ; SHARP PA In: PROC NATL ACAD SCI USA 74(8):3171-5, AUG 77 Support source(s): AMERICAN CANCER SOCIETY CANCER INSTITUTE Corporate Address: MIT, CAMBRIDGE
4	163					2	31	56	74	BINDING OF SOLUBLE FORM OF FIBROBLAST SURFACE PROTEIN, FIBRONECTIN, TO COLLAGEN. By: ENGVALL E ; RUOSLAHTI E In: INT J CANCER 20(1):1-5, 15 JUL 77 Support source(s): PRIVATE NON-PROFIT CANCER INSTITUTE Corporate Address: CITY HOPE MED CTR
5	146					2	38	49	57	BETA-ENDORPHIN AND ADRENOCORTICOTROPIN ARE SELECTED CONCOMITANTLY BY THE PITUITARY GLAND. By: GUILLEMIN R ; VARGO T ; ROSSIER J ; MINICK S ; LING N ; RIVIER C VALE W ; BLOOM F In: SCIENCE 197(4311):1367-9, 30 SEP 77 Support source(s): ARTHR & METABOL DIS CHILD HEALTH & HUMAN DEV PRIVATE NON-PROFIT Corporate Address: SALK INST BIOL

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 10 (Continued)

The Ten 1977 U.S. Papers with Non-Federal
Support Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	144				*	1	5	48	90	METHOD FOR DETECTION OF SPECIFIC RNAS IN AGAROSE GELS BY TRANSFER TO DIAZOBENZYLOXYMETHYL-PAPER AND HYBRIDIZATION WITH DNA PROBES. By: ALWINE JC ; KEMP DJ ; STARK GR In: PROC NATL ACAD SCI USA 74(12):5350-4, DEC 77 Support source(s): CANCER INSTITUTE AMERICAN CANCER SOCIETY Corporate Address: STANFORD U MED
7	137					2	18	53	64	ENDOCYTOSIS. By: SILVERSTEIN SC ; STEINMAN RM ; COHN ZA In: ANNU REV BIOCHEM 46:669-722, 1977 Support source(s): AMERICAN HEART ASSOC ALLERG & INFECT DISEASES Corporate Address: ROCKFLR U, NY
8	120					1	24	45	50	PHOSPHODIESTERASE PROTEIN ACTIVATOR MIMICS RED BLOOD CELL CYTOPLASMIC ACTIVATOR OF (CA2+-MG2+)ATPASE. By: GOPINATH RM ; VINCENZI FF In: BIOCHEM BIOPHYS RES COMMUN 77(4):1203-9, 22 AUG 77 Support source(s): PRIVATE NON-PROFIT ARTHR & METABOL DIS Corporate Address: U WASH MED
9	110					6	12	32	60	SCREENING LAMBDAGT RECOMBINANT CLONES BY HYBRIDIZATION TO SINGLE PLAQUES IN SITU. By: BENTON WD ; DAVIS RW In: SCIENCE 196(4286):180-2, 8 APR 77 Support source(s): NATL SCIENCE FOUNDATION GENERAL MEDICAL SCIENCES PRIVATE NON-PROFIT Corporate Address: STANFORD U MED
10	109					2	22	43	42	PHOSPHOHEXOSYL COMPONENTS OF A LYSOSOMAL ENZYME ARE RECOGNIZED BY PINOCYTOSIS RECEPTORS ON HUMAN FIBROBLASTS. By: KAPLAN A ; ACHORD DT ; SLY WS In: PROC NATL ACAD SCI USA 74(5):2026-30, MAY 77 Support source(s): GENERAL MEDICAL SCIENCES PRIVATE NON-PROFIT Corporate Address: ST LOUIS U MED WASHINGTON U MED

APPENDIX B

Table 11

The Ten 1973 U.S. Papers with Support Unacknowledged Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	821	2	53	104	112	144	153	140	113	ANALYSIS OF BACTERIOPHAGE T7 EARLY RNAS AND PROTEINS ON SLAB GELS. By: STUDIER FW In: J MOL BIOL 79(2):237-48, 15 SEP 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: BROOKHVN LABS
2	412	5	30	46	61	72	64	72	62	FLUOROMETRIC ASSAY OF PROTEINS IN THE NANOGRAM RANGE. By: B OHLEN P ; STEIN S ; DAIRMAN W ; UDENFRIEND S In: ARCH BIOCHEM BIOPHYS 155(1):213-20, MAR 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
3	238	1	8	29	52	43	47	37	21	THIN-LAYER CHROMATOGRAPHY OF SUB-NANOMOLE AMOUNTS OF PHENYLTHIOHYDANTOIN (PTH) AMINO ACIDS ON POLYAMIDE SHEETS. By: SUMMERS MR ; SMYTHERS GW ; OROSZLAN S In: ANAL BIOCHEM 53(2):624-8, JUN 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
4	222	0	3	23	39	32	36	54	35	A SIMPLIFIED METHOD FOR THE QUANTITATIVE ASSAY OF SMALL AMOUNTS OF PROTEIN IN BIOLOGIC MATERIAL. By: SCHACTERLE GR ; POLLACK RL In: ANAL BIOCHEM 51(2):654-5, FEB 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: TEMPLE U MED
5	215	0	46	56	36	27	26	15	9	BIOGENESIS OF MRNA: GENETIC REGULATION IN MAMMALIAN CELLS. By: DARNELL JE ; JELINEK WR ; MOLLOY GR In: SCIENCE 181(106):1215-21, 28 SEP 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: COLUMBIA, NYC
6	190	0	4	31	18	31	42	34	30	VOLTAGE CLAMP ANALYSIS OF ACETYLCHOLINE PRODUCED END-PLATE CURRENT FLUCTUATIONS AT FROG NEUROMUSCULAR JUNCTION. By: ANDERSON CR ; STEVENS CF In: J PHYSIOL (LOND) 235(3):655-91, DEC 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U WASH MED
7	166	8	51	41	21	17	12	11	5	SURFACE CHANGES IN TRANSFORMED CELLS DETECTED BY LECTINS. By: BURGER MM In: FED PROC 32(1):91-101, JAN 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: PRINCETON U

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 11 (Continued)

The Ten 1973 U.S. Papers with Support Unacknowledged Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
8	161	0	7	12	18	29	28	37	30	A SIMPLE PROCEDURE FOR REMOVAL OF TRITON X-100 FROM PROTEIN SAMPLES. By: HOLLOWAY PW In: ANAL BIOCHEM 53(1):304-8, MAY 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U VA MED
9	140	0	8	23	15	16	22	21	35	IMPROVED ESTIMATION OF SECONDARY STRUCTURE IN RIBONUCLEIC ACIDS. By: TINOCO I JR ; BORER PN ; DENGLER B ; LEVIN MD ; UHLENBECK OC CROTHERS DM ; BRALLA J In: NATURE NEW BIOL 246(150):40-1, 14 NOV 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CAL, BERKLY YALE U, N HAVEN U ILL, URBANA
10	136	0	12	19	26	33	13	25	8	TOWARD MOLECULAR MECHANISMS OF DEVELOPMENTAL PROCESSES. By: RUTTER WJ ; PICTET RL ; MORRIS PW In: ANNU REV BIOCHEM 42:601-46, 1973 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CAL MED, S FRAN

APPENDIX B

Table 12

The Ten 1974 U.S. Papers with Support
Unacknowledged Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	466		4	40	89	88	93	87	65	THE ORGANIZATION OF PROTEINS IN THE HUMAN RED BLOOD CELL MEMBRANE. A REVIEW. By: STECK TL In: J CELL BIOL 62(1):1-19, JUL 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CHIC PRITZ MED
2	376		1	42	96	67	61	61	48	THE MOLECULAR ORGANIZATION OF MEMBRANES. By: SINGER SJ In: ANNU REV BIOCHEM 43(0):805-33, 1974 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CAL, SAN DIEGO
3	328		15	59	58	75	50	42	29	FEMALE STEROID HORMONES AND TARGET CELL NUCLEI. By: O'MALLEY BW ; MEANS AR In: SCIENCE 183(125):610-20, 15 FEB 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: BAYLOR U, HOUSTON (MED)
4	194		1	13	26	38	42	43	31	IMMUNOLOGIC CHARACTERIZATION OF HUMAN MALIGNANT LYMPHOMAS. By: LUKES RJ ; COLLINS RD In: CANCER 34(4 SUPPL):SUPPL:1488-503, OCT 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: USC MED, LA
4	194		5	45	36	38	31	19	20	INTERACTION OF DRUGS WITH MICROTUBULE PROTEINS. By: WILSON L ; BAMBURG JR ; MIZEL SB ; GRISHAM LM ; CRESWELL KM In: FED PROC 33(2):158-66, FEB 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: STANFORD U MED
6	192		2	25	32	32	40	35	26	THE SODIUM-POTASSIUM ADENOSINETRIPHOSPHATASE. By: DAHL JL ; HOKIN LE In: ANNU REV BIOCHEM 43(0):327-56, 1974 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U WISC MED
7	189		8	30	40	44	36	25	6	A PROPOSED NOMENCLATURE FOR THE VIRION PROTEINS OF ONCOGENIC RNA VIRUSES. By: AUGUST JT ; BOLOGNESI DP ; FLEISSNER E ; GILDEN RV ; NOWINSKI RC In: VIROLOGY 60(2):595-600, AUG 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: SLOAN-KTRG CANC RES INST, NY DUKE MED UNIDENTIFIED

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 12 (Continued)

The Ten 1974 U.S. Papers with Support
Unacknowledged Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
8	163		7	43	51	33	16	7	6	COMPUTERIZED AXIAL TOMOGRAPHY WITH THE EMI SCANNER. By: NEW PF ; SCOTT WR ; SCHNUR JA ; DAVIS KR ; TAVERAS JM In: RADIOLOGY 110(1):109-23, JAN 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: HARVARD MED MASS GEN HOSP, BOS
9	156		3	28	46	19	28	23	9	EUKARYOTIC MESSENGER RNA. By: BRAWERMAN G In: ANNU REV BIOCHEM 43(0):621-42, 1974 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: TUFTS MED, BOS
10	152		2	23	26	33	31	24	13	THE SELECTIVITY OF TRANSCRIPTION. By: CHAMBERLIN MJ In: ANNU REV BIOCHEM 43(0):721-75, 1974 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CAL, BERKLY

APPENDIX B

Table 13

The Ten 1975 U.S. Papers with Support Unacknowledged Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	312			4	33	49	65	80	81	INTRACELLULAR ASPECTS OF THE PROCESS OF PROTEIN SYNTHESIS. By: PALADE G In: SCIENCE 189(4200):347-58, 1 AUG 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: YALE U MED
2	303			1	36	70	53	86	57	PROTEIN PHOSPHORYLATION. By: RUBIN CS ; ROSEN OM In: ANNU REV BIOCHEM 44:831-87, 1975 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: ALB EINST, YESHIVA
3	247			1	26	55	66	66	33	CHEMICAL CARCINOGENESIS. By: HEIDELBERGER C In: ANNU REV BIOCHEM 44:79-121, 1975 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U WISC MED
4	237			0	43	64	49	47	34	FREEZE-ETCHING NOMENCLATURE. By: BRANTON D ; BULLIVANT S ; GILULA NB ; KARNOVSKY MJ ; MOOR H M UHLETHALER K ; NORTHCOTE DH ; PACKER L ; SATIR B ; SATIR P SPETH V ; STAEHLIN LA ; STEERE RL ; WEINSTEIN RS In: SCIENCE 190(4209):54-6, 3 OCT 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: HARVARD MED ROCKFLR U, NY FOREIGN
5	199			2	19	46	41	50	41	COMPLEMENT. By: M ULLER-EBERHARD HJ In: ANNU REV BIOCHEM 44:697-724, 1975 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: SCRIPPS CLINIC
6	175			19	57	42	26	24	7	METHYLATION-DEPENDENT TRANSLATION OF VIRAL MESSENGER RNAS IN VITRO. By: BOTH GW ; BANERJEE AK ; SHATKIN AJ In: PROC NATL ACAD SCI USA 72(3):1189-93, MAR 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED

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*BID-SCI journal set citing BID-MEDLARS papers.

APPENDIX B

Table 13 (Continued)

The Ten 1975 U.S. Papers with Support Unacknowledged Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	168			15	58	45	25	19	6	5'-TERMINAL 7-METHYLGUANOSINE IN EUKARYOTIC MRNA IS REQUIRED FOR TRANSLATION. By: MUTHUKRISHNAN S ; BOTH GW ; FURUICHI Y ; SHATKIN AJ In: NATURE 255(5503):33-7, 1 MAY 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
8	154			1	12	26	37	39	39	REGENERATION OF AMINO ACIDS FROM THIAZOLINONES FORMED IN THE EDMAN DEGRADATION. By: MENDEZ E ; LAI CY In: ANAL BIOCHEM 68(1):47-53, SEP 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
9	153			2	13	36	31	31	40	SUPEROXIDE DISMUTASES. By: FRIDOVICH I In: ANNU REV BIOCHEM 44:147-59, 1975 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: DUKE MED
10	141			27	52	33	10	11	8	REOVIRUS MESSENGER RNA CONTAINS A METHYLATED, BLOCKED 5'-TERMINAL STRUCTURE: M-7G(5')PPP(5')G-MPCP-. By: FURUICHI Y ; MORGAN M ; MUTHUKRISHNAN S ; SHATKIN AJ In: PROC NATL ACAD SCI USA 72(1):362-6, JAN 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED

APPENDIX B

Table 14

The Ten 1976 U.S. Papers with Support Unacknowledged Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	212				2	19	46	93	52	COMPARATIVE ASPECTS OF GLYCOPROTEIN STRUCTURE. By: KORNFELD R ; KORNFELD S In: ANNU REV BIOCHEM 45:217-37, 1976 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: WASHINGTON U MED
2	179				1	18	38	60	62	125I-LABELED HUMAN EPIDERMAL GROWTH FACTOR. BINDING, INTERNALIZATION, AND DEGRADATION IN HUMAN FIBROBLASTS. By: CARPENTER G ; COHEN S In: J CELL BIOL 71(1):159-71, OCT 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: VANDRBLT MED
3	164				8	40	41	44	31	POSSIBLE ROLE FOR CYCLIC NUCLEOTIDES AND PHOSPHORYLATED MEMBRANE PROTEINS IN POSTSYNAPTIC ACTIONS OF NEUROTRANSMITTERS. By: GREENGARD P In: NATURE 260(5547):101-8, 11 MAR 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: YALE U MED
4	163				1	30	47	50	35	MECHANISMS REGULATING RENIN RELEASE. By: DAVIS JO ; FREEMAN RH In: PHYSIOL REV 56(1):1-56, JAN 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U MO, COMB MED
5	144				19	40	36	30	19	ANALGESIA INDUCED IN VIVO BY CENTRAL ADMINISTRATION OF ENKEPHALIN IN RAT. By: BELLUZZI JD ; GRANT N ; GARSKY V ; SARANTAKIS D ; WISE CD ; STEIN L In: NATURE 260(5552):625-6, 15APR 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
6	109				2	25	24	33	25	THE ELECTROCHEMICAL GRADIENT OF PROTONS AND ITS RELATIONSHIP TO ACTIVE TRANSPORT IN ESCHERICHIA COLI MEMBRANE VESICLES. By: RAMOS S ; SCHULDINER S ; KABACK HR In: PROC NATL ACAD SCI USA 73(6):1892-6, JUN 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 14 (Continued)

The Ten 1976 U.S. Papers with Support
Unacknowledged Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	103				12	20	22	31	18	MULTIPLE FORMS OF RAT LIVER CYTOCHROME P-450. IMMUNOCHEMICAL EVIDENCE WITH ANTIBODY AGAINST CYTOCHROME P-448. By: THOMAS PE ; LU AY ; RYAN D ; WEST SB ; KAWALEK J ; LEVIN W In: J BIOL CHEM 251(5):1385-91, 10 MAR 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
8	93				2	10	20	34	27	GLUTATHIONE AND RELATED GAMMA-GLUTAMYL COMPOUNDS: BIOSYNTHESIS AND UTILIZATION. By: MEISTER A ; TATE SS In: ANNU REV BIOCHEM 45:559-604, 1976 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: CORNELL MED, NYC
9	88				0	16	25	23	24	STEROID RECEPTORS: ELEMENTS FOR MODULATION OF EUKARYOTIC TRANSCRIPTION. By: YAMAMOTO KR ; ALBERTS BM In: ANNU REV BIOCHEM 45:721-46, 1976 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U CAL MED, S FRAN PRINCETON U
10	87				0	11	28	27	21	INVESTIGATION OF PHASE TRANSITIONS OF LIPIDS AND LIPID MIXTURES BY SENSITIVITY DIFFERENTIAL SCANNING CALORIMETRY. By: MABREY S ; STURTEVANT JM In: PROC NATL ACAD SCI USA 73(11):3862-6, NOV 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: YALE U, N HAVEN YALE U MED

APPENDIX B

Table 15

The Ten 1977 U.S. Papers with Support Unacknowledged Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
1	228					12	49	80	87	STRUCTURE OF CHROMATIN. By: KORNBERG RD In: ANNU REV BIOCHEM 46:931-54, 1977 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: HARVARD MED
2	181					6	29	79	67	THE LOW-DENSITY LIPOPROTEIN PATHWAY AND ITS RELATION TO ATHEROSCLEROSIS. By: GOLDSTEIN JL ; BROWN MS In: ANNU REV BIOCHEM 46:897-930, 1977 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U TEX, COMB MED
3	133					1	27	49	56	RELATIONSHIPS BETWEEN CALCIUM AND CYCLIC NUCLEOTIDES IN CELL ACTIVATION. By: RASMUSSEN H ; GOODMAN DB In: PHYSIOL REV 57(3):421-509, JUL 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: YALE U MED
4	113					1	30	36	46	CYCLIC GMP METABOLISM AND INVOLVEMENT IN BIOLOGICAL REGULATION. By: GOLDBERG ND ; HADDOX MK In: ANNU REV BIOCHEM 46:823-96, 1977 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: U MINN, DULUTH, COMB MED
5	103					0	13	45	45	SIMULTANEOUS SINGLE ISOTOPE RADIOENZYMATIC ASSAY OF PLASMA NOREPINEPHRINE, EPINEPHRINE AND DOPAMINE. By: PEULER JD ; JOHNSON GA In: LIFE SCI 21(5):625-36, 1 SEP 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
5	103					1	32	35	35	EUKARYOTIC DNA POLYMERASES. By: WEISSBACH A In: ANNU REV BIOCHEM 46:25-47, 1977 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
7	101					2	14	58	27	LEGIONNAIRES' DISEASE: ISOLATION OF A BACTERIUM AND DEMONSTRATION OF ITS ROLE IN OTHER RESPIRATORY DISEASE. By: MCDADE JE ; SHEPARD CC ; FRASER DW ; TSAI TR ; REDUS MA ; DOWDLE WR In: N ENGL J MED 297(22):1197-203, 1 DEC 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: CTR DIS CNTROL

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 15 (Continued)

The Ten 1977 U.S. Papers with Support
Unacknowledged Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	101				*	3	30	49	19	CYCLIC NUCLEOTIDES AND NERVOUS SYSTEM FUNCTION. By: NATHANSON JA In: PHYSIOL REV 57(2):157-256, APR 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: NIMH-ST. ELIZ
9	94					5	23	32	34	DESIGN OF SPECIFIC INHIBITORS OF ANGIOTENSIN-CONVERTING ENZYME: NEW CLASS OF ORALLY ACTIVE ANTIHYPERTENSIVE AGENTS. By: ONDETTI MA ; RUBIN B ; CUSHMAN DW In: SCIENCE 196(4288):441-4, 22 APR 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: UNIDENTIFIED
10	92					2	17	52	21	LEGIONNAIRES' DISEASE: DESCRIPTION OF AN EPIDEMIC OF PNEUMONIA. By: FRASER DW ; TSAI TR ; ORENSTEIN W ; PARKIN WE ; BEECHAM HJ SHARRAR RG ; HARRIS J ; MALLISON GF ; MARTIN SM ; MCDADE JE SHEPARD CC ; BRACHMAN PS In: N ENGL J MED 297(22):1189-97, 1 DEC 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: CTR DIS CNTROL

APPENDIX B

Table 16

The Ten 1973 Foreign Papers (No U.S. Support) Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year								
		73	74	75	76	77	78	79	80	
1	509	1	18	43	88	92	92	106	69	EFFICIENT TRANSLATION OF TOBACCO MOSAIC VIRUS RNA AND RABBIT GLOBIN 9S RNA IN A CELL-FREE SYSTEM FROM COMMERCIAL WHEAT GERM. By: ROBERTS BE ; PATERSON BM In: PROC NATL ACAD SCI USA 70(8):2330-4, AUG 73 Support source(s): NATL SCIENCE FOUNDATION Corporate Address: FOREIGN
2	396	5	43	42	66	73	62	48	57	CELLULAR LOCALIZATION OF AN EPSTEIN-BARR VIRUS (EBV)-ASSOCIATED COMPLEMENT-FIXING ANTIGEN IN PRODUCER AND NON-PRODUCER LYMPHOBLASTOID CELL LINES. By: REEDMAN BM ; KLEIN G In: INT J CANCER 11(3):499-520, MAY 73 Support source(s): CANCER INSTITUTE Corporate Address: FOREIGN
3	351	0	1	17	27	43	66	98	99	THE LABELLING OF PROTEINS TO HIGH SPECIFIC RADIOACTIVITIES BY CONJUGATION TO A 125I-CONTAINING ACYLATING AGENT. By: BOLTON AE ; HUNTER WM In: BIOCHEM J 133(3):529-39, JUL 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
4	339	2	49	53	58	53	51	42	31	THE BIOCHEMISTRY OF PLANT LECTINS (PHYTOHEMAGGLUTININS). By: LIS H ; SHARON N In: ANNU REV BIOCHEM 42(0):541-74, 1973 Support source(s): LIBRARY OF MEDICINE NATL INSTITUTE OF HEALTH-GENL DEPT OF AGRICULTURE Corporate Address: FOREIGN
4	339	7	38	48	57	63	55	54	33	PURIFICATION AND FURTHER PROPERTIES OF SINGLE-STRAND-SPECIFIC NUCLEASE FROM ASPERGILLUS ORYZAE. By: VOGT VM In: EUR J BIOCHEM 33(1):192-200, 15 FEB 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
6	279	0	4	15	33	59	56	60	52	A RAPID, SENSITIVE, AND SPECIFIC METHOD FOR THE DETERMINATION OF PROTEIN IN DILUTE SOLUTION. By: SCHAFFNER W ; WEISSMANN C In: ANAL BIOCHEM 56(2):502-14, DEC 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 16 (Continued)

The Ten 1973 Foreign Papers (No U.S. Support) Most Highly Cited in 1973-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	273	0	13	30	45	40	64	47	34	ALTERATION OF CELL-SURFACE PROTEINS BY VIRAL TRANSFORMATION AND BY PROTEOLYSIS. By: HYNES RO In: PROC NATL ACAD SCI USA 70(11):3170-4, NOV 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
8	261	2	8	33	48	71	40	32	27	CHROMATIN SUB-STRUCTURE. THE DIGESTION OF CHROMATIN DNA AT REGULARLY SPACED SITES BY A NUCLEAR DEOXYRIBONUCLEASE. By: HEWISH DR ; BURGOYNE LA In: BIOCHEM BIOPHYS RES COMMUN 52(2):504-10, 15 MAY 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
9	256	0	41	57	53	33	25	25	22	MEMBRANE STRUCTURE: SOME GENERAL PRINCIPLES. By: BRETSCHER MS In: SCIENCE 181(100):622-9, 17 AUG 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
10	215	0	15	23	39	39	34	28	37	ISOLATED REMOVAL OF HYPOTHALAMIC OR OTHER BRAIN NUCLEI OF THE RAT. By: PALKOVITS M In: BRAIN RES 59:449-50, 14 SEP 73 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN

APPENDIX B

Table 17

The Ten 1974 Foreign Papers (No U.S. Support) Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	1668		2	22	101	193	313	505	532	A FILM DETECTION METHOD FOR TRITIUM-LABELLED PROTEINS AND NUCLEIC ACIDS IN POLYACRYLAMIDE GELS. By: BONNER WM ; LASKEY RA In: EUR J BIOCHEM 46(1):83-8, 1 JUL 74 Support source(s): PRIVATE NON-PROFIT ARTHRITIS FOUNDATION Corporate Address: FOREIGN
2	370		8	57	77	96	62	46	24	CHROMATIN STRUCTURE: A REPEATING UNIT OF HISTONES AND DNA. By: KORNBERG RD In: SCIENCE 184(139):868-71, 24 MAY 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
3	277		9	36	53	64	49	39	27	ISOLATION AND STRUCTURE OF TWO PROSTAGLANDIN ENDOPEROXIDES THAT CAUSE PLATELET AGGREGATION. By: HAMBERG M ; SVENSSON J ; WAKABAYASHI T ; SAMUELSSON B In: PROC NATL ACAD SCI USA 71(2):345-9, FEB 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
4	276		0	35	65	77	42	34	23	SUBUNIT STRUCTURE OF CHROMATIN. By: NOLL M In: NATURE 251(5472):249-51, 20 SEP 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
5	265		1	16	38	44	42	66	58	PROSTAGLANDIN ENDOPEROXIDES. NOVEL TRANSFORMATIONS OF ARACHIDONIC ACID IN HUMAN PLATELETS. By: HAMBERG M ; SAMUELSSON B In: PROC NATL ACAD SCI USA 71(9):3400-4, SEP 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
6	243		2	22	33	36	39	59	52	NEW GIEMSA METHOD FOR THE DIFFERENTIAL STAINING OF SISTER CHROMATIDS. By: PERRY P ; WOLFF S In: NATURE 251(5471):156-8, 13 SEP 74 Support source(s): ATOMIC ENERGY COMMISSION(ERDA) Corporate Address: U CAL MED, S FRAN FOREIGN

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 17 (Continued)

The Ten 1974 Foreign Papers (No U.S.
Support) Most Highly Cited in 1974-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
7	228		6	45	55	62	21	27	12	CHROMATIN STRUCTURE; OLIGOMERS OF THE HISTONES. By: KORNBERG RD ; THOMAS JO In: SCIENCE 184(139):865-8, 24 MAY 74 Support source(s): PRIVATE NON-PROFIT Corporate Address: FOREIGN
8	216		3	15	22	37	41	54	44	THE DIRECT LINEAR PLOT. A NEW GRAPHICAL PROCEDURE FOR ESTIMATING ENZYME KINETIC PARAMETERS. By: EISENTHAL R ; CORNISH-BOWDEN A In: BIOCHEM J 139(3):715-20, JUN 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
9	202		5	19	21	45	37	35	40	THE 3'-TERMINAL SEQUENCE OF ESCHERICHIA COLI 16S RIBOSOMAL RNA: COMPLEMENTARITY TO NONSENSE TRIPLETS AND RIBOSOME BINDING SITES. By: SHINE J ; DALGARNO L In: PROC NATL ACAD SCI USA 71(4):1342-6, APR 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
10	183		1	8	31	30	39	42	32	DIFFERENCE IN MICROVISCOSITY INDUCED BY DIFFERENT CHOLESTEROL LEVELS IN THE SURFACE MEMBRANE LIPID LAYER OF NORMAL LYMPHOCYTES AND MALIGNANT LYMPHOMA CELLS. By: SHINITZKY M ; INBAR M In: J MOL BIOL 85(4):603-15, 5 JAN 74 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN

APPENDIX B

Table 18

The Ten 1975 Foreign Papers (No U.S. Support) Most Highly Cited in 1975-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	956			0	20	73	159	297	407	DETECTION OF SPECIFIC SEQUENCES AMONG DNA FRAGMENTS SEPARATED BY GEL ELECTROPHORESIS. By: SOUTHERN EM In: J MOL BIOL 98(3):503-17, 5 NOV 75 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN
2	869			0	30	112	186	271	270	QUANTITATIVE FILM DETECTION OF 3H AND 14C IN POLYACRYLAMIDE GELS BY FLUOROGRAPHY. By: LASKEY RA ; MILLS AD In: EUR J BIOCHEM 56(2):335-41, 15 AUG 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
3	535			0	91	132	121	101	90	IDENTIFICATION OF TWO RELATED PENTAPEPTIDES FROM THE BRAIN WITH POTENT OPIATE AGONIST ACTIVITY. By: HUGHES J ; SMITH TW ; KOSTERLITZ HW ; FOTHERGILL LA ; MORGAN BA MORRIS HR In: NATURE 258(5536):577-80, 18 DEC 75 Support source(s): NATL INST DRUG ABUSE (NIDA) FOREIGN GOVERNMENT Corporate Address: FOREIGN
4	421			3	73	69	87	99	90	SOLUBILIZATION OF MEMBRANES BY DETERGENTS. By: HELENIUS A ; SIMONS K In: BIOCHIM BIOPHYS ACTA 415(1):29-79, 25 MAR 75 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN
5	347			0	30	82	85	75	75	THROMBOXANES: A NEW GROUP OF BIOLOGICALLY ACTIVE COMPOUNDS DERIVED FROM PROSTAGLANDIN ENDOPEROXIDES. By: HAMBERG M ; SVENSSON J ; SAMUELSSON B In: PROC NATL ACAD SCI USA 72(8):2994-8, AUG 75 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN
6	267			0	6	8	14	63	176	CONTINUOUS CULTURES OF FUSED CELLS SECRETING ANTIBODY OF PREDEFINED SPECIFICITY. By: K OHLER G ; MILSTEIN C In: NATURE 256(5517):495-7, 7 AUG 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 18 (Continued)

The Ten 1975 Foreign Papers (No U.S.
Support) Most Highly Cited in 1975-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
		Cites received by citing year								
7	237			0	43	64	49	47	34	FREEZE-ETCHING NOMENCLATURE. By: BRANTON D ; BULLIVANT S ; GILULA NB ; KARNOVSKY MJ ; MOOR H M UHLETHALER K ; NORTHCOTE DH ; PACKER L ; SATIR B ; SATIR P SPETH V ; STAEHLIN LA ; STEERE RL ; WEINSTEIN RS In: SCIENCE 190(4209):54-6, 3 OCT 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: HARVARD MED ROCKFLR U, NY FOREIGN
8	225			4	16	27	54	68	56	PLASMA-HIGH-DENSITY-LIPOPROTEIN CONCENTRATION AND DEVELOPMENT OF ISCHAEMIC HEART-DISEASE. By: MILLER GJ ; MILLER NE In: LANCET 1(7897):16-9, 4 JAN 75 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
9	224			14	51	53	43	32	31	ISOLATION OF AN ENDOGENOUS COMPOUND FROM THE BRAIN WITH PHARMACOLOGICAL PROPERTIES SIMILAR TO MORPHINE. By: HUGHES J In: BRAIN RES 88(2):295-308, 2 MAY 75 Support source(s): NATL INST MENTAL HEALTH FOREIGN GOVERNMENT Corporate Address: FOREIGN
10	207			4	30	33	30	53	57	INOSITOL PHOSPHOLIPIDS AND CELL SURFACE RECEPTOR FUNCTION. By: MICHELL RH In: BIOCHIM BIOPHYS ACTA 415(1):81-47, 25 MAR 75 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN

APPENDIX B

Table 19

The Ten 1976 Foreign Papers (No U.S. Support) Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
1	499				0	40	100	169	190	AN EFFICIENT MRNA-DEPENDENT TRANSLATION SYSTEM FROM RETICULOCYTE LYSATES. By: PELHAM HR ; JACKSON RJ In: EUR J BIOCHEM 67(1):247-56, 1 AUG 76 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN
2	289				0	49	89	77	74	AN ENZYME ISOLATED FROM ARTERIES TRANSFORMS PROSTAGLANDIN ENDOPEROXIDES TO AN UNSTABLE SUBSTANCE THAT INHIBITS PLATELET AGGREGATION. By: MONCADA S ; GRYGLEWSKI R ; BUNTING S ; VANE JR In: NATURE 263(5579):663-5, 21 OCT 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
3	227				21	67	49	52	38	IDENTIFICATION OF MUTAGENIC METABOLITES OF BENZO(A)PYRENE IN MAMMALIAN CELLS. By: HUBERMAN E ; SACHS L ; YANG SK ; GELBOIN V In: PROC NATL ACAD SCI USA 73(2):607-11, FEB 76 Support source(s): CANCER INSTITUTE Corporate Address: NIH FOREIGN
4	142				5	19	25	39	54	DETECTION OF IMMUNE COMPLEXES IN UNHEATED SERA BY MODIFIED 125I-CLQ BINDING TEST. EFFECT OF HEATING ON THE BINDING OF CLQ BY IMMUNE COMPLEXES AND APPLICATION OF THE TEST TO SYSTEMIC LUPUS ERYTHEMATOSU By: ZUBLER RH ; LANGE G ; LAMBERT PH ; MIESCHER PA In: J IMMUNOL 116(1):232-5, JAN 76 Support source(s): FOREIGN GOVERNMENT UN+SUPRANATIONAL ORGS Corporate Address: FOREIGN
5	137				0	24	41	44	28	THE RED CELL MEMBRANE. By: MARCHESI VT ; FURTHMAYR H ; TOMITA M In: ANNU REV BIOCHEM 45:667-98, 1976 Support source(s): GENERAL MEDICAL SCIENCES Corporate Address: YALE U MED FOREIGN

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 19 (Continued)

The Ten 1976 Foreign Papers (No U.S.
Support) Most Highly Cited in 1976-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	136			*	7	34	39	30	26	PROPERTIES OF THE ANTIGEN-SPECIFIC SUPPRESSIVE T-CELL FACTOR IN THE REGULATION OF ANTIBODY RESPONSE OF THE MOUSE. IV. SPECIAL SUBREGION ASSIGNMENT OF THE GENE(S) THAT CODES FOR THE SUPPRESSIVE T-CELL By: TADA T ; TANIGUCHI M ; DAVID CS In: J EXP MED 144(3):713-25, 1 SEP 76 Support source(s): FOREIGN GOVERNMENT AMERICAN CANCER SOCIETY Corporate Address: WASHINGTON U MED FOREIGN
6	136				0	11	32	47	46	SUBPOPULATIONS OF HUMAN T CELLS IDENTIFIED BY RECEPTORS FOR IMMUNOGLOBULINS AND MITOGEN RESPONSIVENESS. By: MORETTA L ; FERRARINI M ; MINGARI MC ; MORETTA A ; WEBB SR In: J IMMUNOL 117(6):2171-4, DEC 76 Support source(s): ALLERG & INFECT DISEASES CANCER INSTITUTE CHILD HEALTH & HUMAN DEV Corporate Address: U ALAB MED, BRMGH FOREIGN
8	131				5	25	39	33	29	MICROVISCOSITY PARAMETERS AND PROTEIN MOBILITY IN BIOLOGICAL MEMBRANES. By: SHINITZKY M ; INBAR M In: BIOCHIM BIOPHYS ACTA 433(1):133-49, 16 APR 76 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN
9	121				2	32	24	33	30	SOLENOIDAL MODEL FOR SUPERSTRUCTURE IN CHROMATIN. By: FINCH JT ; KLUG A In: PROC NATL ACAD SCI USA 73(6):1897-901, JUN 76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
10	120				0	11	31	34	44	THE FUNCTION OF STEROLS IN MEMBRANES. By: DEMEL RA ; DE KRUYFF B In: BIOCHIM BIOPHYS ACTA 457(2):109-32, 26OCT76 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN

APPENDIX B

Table 20

The Ten 1977 Foreign Papers (No U.S. Support) Most Highly Cited in 1977-80*

Rank	Total Cites Received	73	74	75	76	77	78	79	80	
		Cites received by citing year								
1	283				*	37	108	76	62	NUCLIOTIDE SEQUENCE OF BACTERIOPHAGE PHI X174 DNA. By: SANGER F ; AIR GM ; BARRELL BG ; BROWN NL ; COULSON AR ; FIDDES CA HUTCHISON CA ; SLOCOMBE PM ; SMITH M In: NATURE 265(5596):687-95, 24 FEB 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
2	154					8	38	55	53	BENZODIAZEPINE RECEPTORS IN RAT BRAIN. By: SQUIRES RF ; BRASTRUP C In: NATURE 266(5604):732-4, 21 APR 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
3	148					3	25	47	73	ENDOGENOUS OPIOID PEPTIDES: MULTIPLE AGONISTS AND RECEPTORS. By: LORD JA ; WATERFIELD AA ; HUGHES J ; KOSTERLITZ HW In: NATURE 267(5611):495-9, 9 JUN 77 Support source(s): FOREIGN GOVERNMENT NATL INST DRUG ABUSE (NIDA) OTHER FEDERAL GOVERNMENT Corporate Address: FOREIGN
4	135					30	31	41	33	ACTION OF MICROCOCCAL NUCLEASE ON CHROMATIN AND THE LOCATION OF HISTONE H1. By: NOLL M ; KORNBERG RD In: J MOL BIOL 109(3):393-404, 25 JAN 77 Support source(s): FOREIGN GOVERNMENT Corporate Address: FOREIGN
5	123					9	29	59	26	CELL-FREE TRANSLATION OF SIMIAN VIRUS 40 EARLY MESSENGER RNA CODING FOR VIRAL T-ANTIGEN. By: PRIVES C ; GILBOA E ; REVEL M ; WINOCOUR E In: PROC NATL ACAD SCI USA 74(2):457-61, FEB 77 Support source(s): CANCER INSTITUTE Corporate Address: FOREIGN
6	118					6	36	44	32	STRUCTURE OF NUCLEOSOME CORE PARTICLES OF CHROMATIN. By: FINCH JT ; LUTTER LC ; RHODES D ; BROWN RS ; RUSHTON B ; LEVITT M KLUG A In: NATURE 269(5623):29-36, 1 SEP 77 Support source(s): NATL INSTITUTE OF HEALTH-GENL Corporate Address: FOREIGN

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*BID-SCI journal set citing BID-MEDLINE papers.

APPENDIX B

Table 20 (Continued)

The Ten 1977 Foreign Papers (No U.S.
Support) Most Highly Cited in 1977-80*

Rank	Total Cites Received	Cites received by citing year 73	74	75	76	77	78	79	80	
6	118					0	25	49	44	BENZODIAZEPINE RECEPTOR: DEMONSTRATION IN THE CENTRAL NERVOUS SYSTEM. By: M OHLER H ; OKADA T In: SCIENCE 198(4319):849-51, 25 NOV 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
8	110					0	18	45	47	DNA SEQUENCING WITH CHAIN-TERMINATING INHIBITORS. By: SANGER F ; NICKLEN S ; COULSON AR In: PROC NATL ACAD SCI USA 74(12):5463-7, DEC 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN
9	102					0	8	39	55	ANALYSIS OF SINGLE- AND DOUBLE-STRANDED NUCLEIC ACIDS ON POLYACRYLAMIDE AND AGAROSE GELS BY USING GLYOXAL AND ACRIDINE ORANGE. By: MCMASTER GK ; CARMICHAEL GG In: PROC NATL ACAD SCI USA 74(11):4835-8, NOV 77 Support source(s): NATL SCIENCE FOUNDATION PRIVATE NON-PROFIT Corporate Address: FOREIGN
10	98					0	16	32	50	ENHANCED AUTORADIOGRAPHIC DETECTION OF 32P AND 125I USING INTENSIFYING SCREENS AND HYPERSENSITIZED FILM. By: LASKEY RA ; MILLS AD In: FEBS LETT 82(2):314-6, 15 OCT 77 Support source(s): ALL UNACKNOWLEDGED/UNIDENTIF. Corporate Address: FOREIGN

APPENDIX C

LISTING OF THE BID-MEDLINE JOURNAL SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED)

FIELD [1]: CLINICAL MEDICINE

GENRL & INTERNAL MED

AM J MED	(L2)
AM J MED SC	(L2)
ANN INT MED	(L1)
ARCH IN MED	(L2)
BIOCHEM MED	(L3)
CLIN CHEM	(L3)
CLIN CHEM A	(L3)
CLIN SC MOL	(L3)
J AM MED A	(L1)
J CHRON DIS	(L1)
J CLIN INV	(L3)
J LA CL MED	(L3)
LANCET	(L2)
MEDICINE	(L2)
N ENG J MED	(L2)
P SOC EXP M	(L3)
SOUTH MED J	(L1)
YALE J BIOL	(L3)

ALLERGY

J ALLERG CL	(L2)

ANESTHESIOLOGY

ANESTH ANAL	(L2)
ANESTHESIOL	(L2)

CANCER

CANC CHEMOT	(L3)
CANCER	(L2)
CANCER RES	(L3)
INT J CANC	(L3)
J NAT CANC	(L3)
ONCOLOGY	(L2)

CARDIOVASCULAR SYSTM

AM HEART J	(L2)
AM J CARD	(L2)
*CHEST	(L1)
CIRCUL RES	(L3)
CIRCULATION	(L2)

DENTISTRY

AM J ORTHOD	(L2)
ARCH ORAL B	(L3)
J AM DENT A	(L1)
J DENT RES	(L3)
J PERIODONT	(L2)
ORAL SURG O	(L2)

DERMAT & VENERL DIS

ARCH DERMAT	(L2)
J INVES DER	(L3)

ENDOCRINOLOGY

DIABETES	(L3)
ENDOCRINOL	(L3)
GEN C ENDO	(L4)
J CLIN END	(L3)
J ENDOCR	(L3)
METABOLISM	(L3)
NEUROENDOCR	(L3)

FERTILITY

FERT STERIL	(L2)
J REPR FERT	(L3)

GASTROENTEROLOGY

DIG DIS SCI	(L2)
GASTROENTY	(L2)

---

*Journal split, or subdivided, between two or more subfields.

xDenotes journal in original BID-SCI 275-journal set but not in the BID-MEDLINE 240-journal set, as a result of coverage changes.

APPENDIX C

LISTING OF THE BID-MEDLINE JOURNAL SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED) (Continued)

FIELD [1]: CLINICAL MEDICINE (Continued)

GERIATRICS

GERIATRICS	(L1)
GERONTOL	(L1)
J AM GER SO	(L1)
J GERONTOL	(L2)

HEMATOLOGY

BLOOD	(L3)
BR J HAEM	(L3)
THROMB DIAT	(L3)
VOX SANGUIN	(L3)

IMMUNOLOGY

CLIN EXP IM	(L2)
IMMUNOLOGY	(L3)
J EXP MED	(L3)
J IMMUNOL	(L3)
J INFEC DIS	(L2)
J RETIC SOC	(L3)
MOL IMMUNOL	(L3)
TRANSPLAN P	(L3)
TRANSPLANT	(L3)

OBSTETRICS & GYNECOL

*AM J OBST G	(L2)
OBSTET GYN	(L1)

NEUROL & NEUROSURG

ARCH NE PSY	(L1)
BRAIN RES	(L4)
DEVELOP MED	(L2)
EEG CL NEUR	(L3)
EPILEPSIA	(L2)
EXP BRAIN R	(L4)
EXP NEUROL	(L4)
J COMP NEUR	(L4)
J NE EXP NE	(L3)
J NE NE PSY	(L2)
J NEUROCHEM	(L4)
J NEUROSURG	(L1)
J NEURPHYSL	(L4)
NEUROLOGY	(L2)
VISION RES	(L4)

OPHTHALMOLOGY

AM J OPHTH	(L2)
ARCH OPHTH	(L2)
EXP EYE RES	(L3)
INV OPHTH V	(L3)

ORTHOPEDICS

CLIN ORTHOP	(L2)
J BONE JOIN	(L1)

ARTHRITIS & RHEUMAT

ANN RHEUM D	(L2)
ARTH RHEUM	(L2)

OTORHINOLARYNGOLOGY

ANN OTOL RH	(L2)
ARCH OTOLAR	(L1)
J SPEECH HE	(L2)
LARYNGOSCOP	(L1)

PATHOLOGY

AM J CLIN P	(L2)
AM J PATH	(L3)
ARCH PATH	(L2)
EXP MOL PAT	(L3)
LAB INV	(L3)

PEDIATRICS

AM J DIS CH	(L2)
BIOL NEONAT	(L3)
J PEDIAT	(L2)
PEDIAT RES	(L3)
PEDIATRICS	(L2)

APPENDIX C

LISTING OF THE BIO-MEDLINE JOURNAL SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED)
(Continued)

FIELD [1]: CLINICAL MEDICINE (Continued)

PHARMACOLOGY

BIOCH PHARM	(L3)
CLIN PHARM	(L2)
CURR THER R	(L1)
EUR J PHARM	(L3)
J CLIN PHAR	(L1)
J PHARM EXP	(L3)
MOLEC PHARM	(L3)
NEUROPHARM	(L3)
PHARM REV	(L3)
PSYCHOPHARM	(L3)
TOX APPL PH	(L3)

PHARMACY

J MED CHEM	(L3)
J PHARM SCI	(L3)

PSYCHIATRY

AM J ORTHOP	(L1)
AM J PSYCHI	(L1)
*ARCH NE PSY	(L1)
BR J PSYCHI	(L1)
xDIS NER SYS	(L1)
J NERV MENT	(L1)
J PSYCH RES	(L2)
PSYCHOS MED	(L2)

RADIOLOGY & NUCL MED

AM J ROENTG	(L1)
INV RADIOL	(L2)
J NUCL MED	(L2)
RADIAT RES	(L4)
RADIOLOGY	(L2)
SEM ROENTG	(L1)

RESPIRATORY SYSTEM

AM R RESP D	(L2)
*CHEST	(L1)
RESP PHYSL	(L4)

SURGERY

AM J SURG	(L1)
ANN SURG	(L1)
ARCH SURG	(L1)
J PED SURG	(L1)
J SURG RES	(L2)
J THOR SURG	(L1)
J TRAUMA	(L1)
PLAS R SURG	(L1)
SURG GYN OB	(L1)
SURGERY	(L1)
T AM S ART	(L1)

TROPICAL MEDICINE

AM J TROP M	(L2)

UROLOGY

INV UROL	(L2)
J UROL	(L1)

NEPHROLOGY

NEPHRON	(L2)

VETERINARY MEDICINE

AM J VET RE	(L3)
J AM VET ME	(L2)

HYGIENE & PUBL HLTH

AM J EPIDEM	(L2)
AM J PUB HE	(L1)
ARCH ENV HE	(L2)
B WHO	(L2)

APPENDIX C

LISTING OF THE BID-MEDLINE JOURNAL SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED)

(Continued)

FIELD [2]: BIOMEDICAL RESEARCH

PHYSIOLOGY

AM J PHYSL	(L4)
ANN R PHYSL	(L4)
J APP PHYSL	(L4)
J GEN PHYSL	(L4)
J PHYSL LON	(L4)
*LIFE SCI	(L4)
PHYSIOL REV	(L4)

ANATOMY & MORPHOLOGY

AM J ANAT	(L4)
ANAT REC	(L4)

EMBRYOLOGY

DEVELOP BIO	(L4)
TERATOLOGY	(L4)

GENETICS & HEREDITY

AM J HU GEN	(L3)
ANN HUM GEN	(L3)
BIOCHEM GEN	(L4)
CHROMOSOMA	(L4)
GENETICS	(L4)
MUTAT RES	(L4)

NUTRITION & DIETET

AM J CLIN N	(L4)
J NUTR	(L4)

BIOCHEM & MOLE BIOL

ANALYT BIOC	(L4)
ANN R BIOCH	(L4)
ARCH BIOCH	(L4)
BIOC BIOP A	(L4)
BIOC BIOP R	(L4)
BIOCHEM	(L4)
BIOCHEM J	(L4)
BIOPOLYMERS	(L4)
COLD S HARB	(L4)
EUR J BIOCH	(L4)
FEBS LETTER	(L4)
J BIOL CHEM	(L4)
J LIPID RES	(L4)
J MOL BIOL	(L4)
J THEOR BIO	(L4)
*LIFE SCI	(L4)
LIPIDS	(L4)
STEROIDS	(L4)

BIOPHYSICS

ANN R BIOPH	(L4)
BIOPHYS J	(L4)
J BIOMECHAN	(L4)

CELL BIOL CYT & HIST

ACT CYTOL	(L2)
CALCIF TISS	(L3)
EXP CELL RE	(L4)
J CELL BIOL	(L4)
J CELL PHYS	(L4)
J HIST CYTO	(L4)
J MEMBR BIO	(L4)
J ULTRA RES	(L4)
STAIN TECH	(L4)

MICROBIOLOGY

ANN R MICRO	(L4)
APPL MICROB	(L4)
J BACT	(L4)
J GEN MICRO	(L4)

APPENDIX C

LISTING OF THE BID-MEDLINE JOURNAL SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED)
(Continued)

FIELD [2]: BIOMEDICAL RESEARCH (Continued)

VIROLOGY

J GEN VIROL	(L4)
J VIROLOGY	(L4)
VIROLOGY	(L4)

PARASITOLOGY

EXP PARASIT	(L4)
J PARASITOL	(L4)
J PROTOZOOL	(L4)

BIOMEDICAL ENGINEERING

COMPUT BIOM	(L3)
IEEE BIOMED	(L3)

MISC BIOMEDICAL RES

HUMAN BIOL	(L3)
LAB ANIM SC	(L3)

GENRL BIOMEDICAL RES

*ANN NY ACAD	(L4)
*EXPERIENTIA	(L4)
*FED PROC	(L4)
*LIFE SCI	(L4)
*NATURE	(L4)
*P NAS US	(L4)
*SCIENCE	(L4)

APPENDIX C

LISTING OF THE BID-MEDLINE JOURNALS SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED)
(Continued)

(BID-MEDLINE JOURNALS IN FIELDS OTHER THAN 1 and 2)

FIELD [3]: BIOLOGY

GENERAL BIOLOGY

*ANN NY ACAD	(L4)
*EXPERIENTIA	(L4)
*NATURE	(L4)
*P NAS US	(L4)
*SCIENCE	(L4)

GENERAL ZOOLOGY

xAM ZOOLOG	(L4)
J EXP ZOOL	(L4)

ENTOMOLOGY

J MED ENT	(L3)

MISCELLANEOUS ZOOL

COMP BIOCH	(L4)

BOTANY

xPHYTOCHEM	(L4)
xPLANT PHYSL	(L4)

AGRICULT & FOOD SCI

J AGR FOOD	(L3)

DAIRY & ANIMAL SCI

J ANIM SCI	(L3)
J DAIRY SCI	(L3)

MISCELLANEOUS BIOL

AM J P ANTH	(L4)

FIELD [4]: CHEMISTRY

ANALYTICAL CHEMISTRY

ANALYT CHEM	(L3)
J CHROMAT	(L3)

ORGANIC CHEMISTRY

CARBOHY RES	(L4)
*xJ CHEM S	(L4)
xJ HETERO CH	(L4)
xJ ORG CHEM	(L4)
xTETRAHEDR L	(L4)

INORGANIC & NUCL CHM

xINORG CHEM	(L4)
xJ CHEM S D	(L4)

GENERAL CHEMISTRY

*ANN NY ACAD	(L4)
*CHEM COMM	(L4)
*EXPERIENTIA	(L4)
xJ AM CHEM S	(L4)
*xJ CHEM S	(L4)
xJ CHEM S CH	(L4)
*NATURE	(L4)
*P NAS US	(L4)
*SCIENCE	(L4)

PHYSICAL CHEMISTRY

xACT CRYST	(L4)
*xJ CHEM S	(L4)
xJ PHYS CHEM	(L4)

APPENDIX C

LISTING OF THE BIO-MEDLINE JOURNAL SET BY FIELD AND SUBFIELD (WITH LEVEL INDICATED)
(Continued)

FIELD [5]: PHYSICS

CHEMICAL PHYSICS

xJ CHEM PHYS	(L4)
*xJ CHEM S	(L4)

ACOUSTICS

xJ ACOUST SO	(L3)

FIELD [8]: PSYCHOLOGY

CLINICAL PSYCHOLOGY

xJ ABN PSYCH	(L1)

PERSONALITY & SOC PS

xJ PERS SOC	(L1)

DEVEL & CHILD PSYCHO

xCHILD DEV	(L2)
xJ EXP C PSY	(L2)

EXPERIMENTAL PSYCHOL

J COM PHYSL	(L4)
J EXP PSYCH	(L4)
NEUROPSYCHO	(L3)
xPERC MOT SK	(L2)
xPERC PSYCH	(L4)
PSYCHOPHYSL	(L3)

GENERAL PSYCHOLOGY

xJ PSYCHOL	(L1)
xPSYCHOL REP	(L2)
*SCIENCE	(L4)

MISC PSYCHOLOGY

AM J MENT D	(L1)

BEHAVIORAL SCIENCE

xBEHAV RES M	(L4)
xJ APPL BE A	(L1)
J EXP AN BE	(L3)
PHYSL BEHAV	(L4)

APPENDIX 5

NATIONAL INSTITUTES OF HEALTH

EVALUATION PLAN

FY 1986

Prepared by the
Office of Program Planning and Evaluation
National Institutes of Health

For Administrative Use

November 1985

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service National Institutes of Health

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National Heart, Lung, and Blood Institute (NHLBI). . . . 6.1

National Institute on Aging (NIA). 7.1

National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) 8.1

National Institute of Allergy and Infectious Diseases (NIAID) 9.1

National Institute of Child Health and Human Development (NICHD). 10.1

National Institute of Dental Research (NIDR) 11.1

National Institute of Environmental Health Sciences (NIEHS). 12.1

National Institute of General Medical Sciences (NIGMS) . 13.1

National Institute of Neurological and Communicative Disorders and Stroke (NINCDS). 14.1

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Introduction

The National Institutes of Health (NIH) 1986 Evaluation Plan is submitted in response to guidance from the Assistant Secretary for Planning and Evaluation. The Plan consists of individual project proposals, forms reporting on studies in progress or recently completed, and budgetary tables. Detailed guidance was provided to participants in the evaluation planning process by the Program Evaluation Branch, Office of Program Planning and Evaluation, NIH (See Appendix A).

As has become customary, the Plan is organized according to the NIH management structure. The NIH-wide chapter includes evaluation projects for the Office of the Director, evaluation projects for Divisions that have no separate appropriation, and other evaluation projects that will be funded by evaluation set-aside funds under criteria discussed below. Each Bureau, Institute and Division (BID) that supports biomedical research extramurally has a separate chapter that contains evaluation project proposals to be supported by program funds. Evaluation Documentation Center (EDC) sheets reporting activities in progress supported by either or both BID and set aside funds are also included in each chapter.

NIH Evaluation Program

The NIH Evaluation Program has the following characteristics:

- Each BID independently designs and develops its own evaluation program. There is no longer a set-aside fund for BID specific evaluations; however, under certain circumstances described below, a BID may manage an evaluation funded from the NIH-wide program.
- The evaluation program budget is composed of set-aside funds tapped for the ASH/ASPE evalution programs and set-aside funds allocated for NIH-wide evaluation projects. BID assessments for the evaluation set-aside fund are proportional to their "appropriations for grants, contracts, or other payments", as required in Section 2113 of the Public Health Service Act.
- The NIH-wide evaluation program may include:
    - Studies of issues that are of NIH-wide concern, such as stabilization, organization of NIH, instrumentation support, scientific support services, etc.

- -- NIH-wide program evaluation such as Small Business Innovative Research, and research and training support mechanisms.
- -- The development of evaluation methods such as measures of research activity.
- -- The design and development of new data bases for program evaluation.
- -- BID evaluations that can be incorporated into NIH-wide studies (e.g., an analysis of a specific BID program as part of a larger study).
- -- BID specific program evaluations that have broad significance for or application to NIH as a whole.*

o An Evaluation Oversight and Policy Committee is chartered by the Director, NIH and consists of a rotating group of BID Directors and NIH Associate and Deputy Directors.

The Committee has three major responsibilities:

- -- Conducting concept review at a policy level of proposals for NIH-wide evaluation studies. This review is to be approved by the Director, NIH, prior to initiation of any study.
- -- Determining the size of the NIH-wide program, which should not exceed 0.25% (1/4 of 1%) of NIH appropriations. The Committee recognizes that special circumstances may arise when the Evaluation Oversight Policy Committee may establish a larger budget.
- -- Making recommendations for new NIH-wide evaluation studies.

o A Technical Merit Review Committee is appointed by the Associate Director for Program Planning and Evaluation to conduct collegial technical review of evaluation proposals.

o The Evaluation Plan contains:

- -- NIH-wide evaluation studies (e.g., studies of NIH-wide concern, NIH-wide programs, and program evaluation methodology);

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*Special consideration may be given proposals from the smaller Institutes, such as NIDR and NLM, which are likely to have fewer proposals that lend themselves to funding as NIH-wide evaluation projects.

- -- BID evaluations included in the NIH-wide program (e.g., BID evaluations that can be incorporated into NIH-wide studies or BID evaluations that have application to NIH as a whole);
- -- BID evaluations reviewed by the NIH-wide Technical Merit Review Committe (e.g., BID evaluations voluntarily submitted by a BID for review by the NIH-wide Technical Review either in addition to a BID technical review or in place of formal technical review by the BID);
- -- BID evaluations not reviewed by the NIH Technical Merit Review Committee (e.g., BID evaluations reviewed by that organization's technical review process).

Review Process

The Technical Merit Review Committee appointed by the Associate Director for Program Planning and Evaluation (ADPPE) for FY 1986 included:

Constance Atwell (NEI)
Martin Blumsack (DRR)
Jack Brown (NIDR)
Sheldon Fishman (OD)
Helen Gee (OD) Chairman
Patricia McKinley (OD)
Cynthia Peters (OD) Executive Secretary
Elliot Siegel (NLM)
Walter Stolz (NIADDK)
Edward Sondik (NCI)

Projects were discussed in review sessions attended by involved evaluation and program staffs. Written critiques were subsequently made available to the proposers to guide them in revising proposals and in making decisions concerning final submission. Overall, the review process resulted in revision of nearly all proposals.

Budget: At the beginning of Chapter 2 is a summary of the FY 1986 NIH evaluation set-aside budget request. It is followed by a complete listing of the FY 1986 NIH evaluation program budget for both set-aside and nonset-aside projects. Contingency funds are included in the request to cover costs of projects not yet ready for submission, or not currently anticipated. Projects costing over $135,000 require ASH/ASPE review and approval. These projects are listed on the next page.

Projects Requiring OASH/ASPE Review
(Over $135,000)

Eval. Project No. Project Title			Budget $ in Thousands			Project	Page
	Prior Yrs	FY 85	FY 86	FY 87	FY 88	Total	No.
NIH 75-1 NAS Continuing Study of National Needs for Biomedical and Behavioral Research Personnel	6,370	581	497 *	495 *	—	7,943	3.35
NIH/DRS 86-304 Productivity Evaluation of the Division of Research Services	—	—	225	150	100	475	3.9
NIH/DRR 86-307 Evaluation of NIH Shared Research Instrumentation Activities (Extramural)	—	—	300	—	—	300	3.16
NIH/NIDR 86-309 Assessment of NIH, Industry, and Academic Relationships in Restorative Materials Research	—	—	250	—	—	250	3.25
NIH/NCI 86-312 Evaluation of the Hospital Cost and Clinical Research Project	—	190 **	—	—	—	190	3.30
NHLBI 86-401 Coronary Heart Disease Risk Factors in Children: Current Physician Attitudes, Knowledge and Practice	—	—	(50)	(150)	(100)	(300)	6.5
NHLBI 86-402 Knowledge, Attitudes, and Behavior of Nurses and Dietitians Regarding Cardiovascular Risk Factors	—	—	(75)	(200)	(75)	(350)	6.8

Notes: * Funds for FY 86 and FY 87 require approval as a continuing project with increased funding requested

** Approved for funding in FY 85

( ) non set-aside funds

2

SUMMARY LIST OF PROJECTS AND BUDGET

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Summary Budget Table

FY 1986 NIH EVALUATION PROGRAM
RECENTLY COMPLETED, ONGOING, AND PROPOSED PROJECTS

Set Aside $ in Thousands; Institute Funds in ( )

BIDs	FY 85	FY 86	FY 87	Future Years
NCI	(834)	(1,121)	(783)	(750)
NEI	(24)	(60)	—	—
NHLBI	(1,174)	(788)	(446)	(260)
NIA	—	(33)	—	—
NIADDK	(2)	(3)	—	—
NIAID	—	—	—	—
NICHD	(42)	(84)	(44)	—
NIDR	(10)	—	—	—
NIEHS	(420)	(292)	(270)	—
NIGMS	—	(20)	(10)	—
NINCDS	(416)	(161)	(62)	—
NLM	(35)	(93)	(10)	—
DRR	—	—	—	—
FIC	—	(150)	—	—
BID TOTAL	(2,957)	(2,805)	(1,625)	(1,010)
OD NIH TOTAL	2,222 (206)	3,000 (232)	1,046 (212)	383 —
NIH TOTAL	2,222 (3,163)	3,000 (3,037)	1,046 (1,837)	383 (1,010)
EVALUATION TOTAL	5,385	6,037	2,883	1,393

EXPLANATORY NOTES AND CODES:

Totals for prior years are only for the projects listed; they are not intended to summarize the program as a whole. Project start dates represent actual or estimated dates funds will be obligated and, if applicable, contract awarded. End dates represent time when final reports were, or will be available, ending the project. Institute supplied funds are enclosed in ( ) and treated as non-adds to set aside funds. C-NYD = Not Yet Determined (Code prior to contract award). TR = Other office or agency. In house includes personal services contracts.

STATUS CODES:

A = Conditionally Approved/Deferred by ASH or ASPE
B = Approved by ASPE
C = Deferred by NIH to Next Fiscal Year
D = ONGOING PROJECTS - Contract Awarded
E = COMPLETE PROJECTS
F = Project Complete But Reports and/or Summary Documentation Not Yet Submitted to ASPE
G = Dropped by NIH
H = Approved by NIH
I = Disapproved by ASH or ASPE
J = Disapproved by NIH
K = Not reviewed by NIH Evaluation Technical Merit Review Committee

Eval. Project No. Contract No. Project Title	Est./Actual Dates (Yr/Mo) Start	Est./Actual Dates (Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
Office of the Director, NIH										
NIH 75-1 (N01-OD-4-2102) NAS Continuing Study of National Needs for Biomedical and Behavioral Research Personnel	74/10	87/10	D	6,370	(64) 581	(75) 497	(80) 495	—	(219) 7,943	3.35
NIH 81-302 (N01-OD-2-2128) Evaluation of Present Strategy for Dissemination of Consensus Development Statements and of the Impact of the Consensus Development Program on the Practice of Medicine. (Impact Study)	81/04	86/02	D	1,193	7	—	—	—	1,200	3.81
NIH 82-302 In house Evaluation of Research Manpower and Training Evaluation Activities	82/05	86/05	D	109	64	10	—	—	183	3.82
NIH 83-301 (N01-OD-1-2109/ N01-OD-5-2118) Evaluation of Biomedical Research Publication Performance	83/09	88/09	D	395	(125) 315	(157) —	(132) —	—	(414) 710	3.83
NIH 83-302 (N01-OD-4-2112) An Evaluation of the Impact of RCDAs on the Recipients of The Awards	83/05	86/10	D	144	165	—	—	—	309	3.85
NIH/FIC 83-302 (N01-TW-3-2118) Evaluation of U.S.-U.S.S.R. Individual Health Scientist Exchange Program	83/09	85/06	E	126	—	—	—	—	126	3.86

	Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Contract No. Project Title	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NIH 83-309 (N01-OD-3-2105) Study of the Organizational Structure of the NIH	83/04	85/02	E	792	—	—	—	—	792	3.87
NIH/DRR 83-310 (N01-RR-3-2112) Alternate Model Systems for Biomedical Research	83/08	85/03	E	400	—	—	—	—	400	3.88
NIH 83-311 (N01-OD-3-2120) Evaluation of Biomedical Research Instrumentation in the U.S.	83/09	85/06	E	200	—	—	—	—	200	3.90
PHS/NIH 83-313 (N01-OD-3-2113) Evaluation of Radioepidemiologic Tables (Radiation-Induced Cancers)	83/07	85/01	E	199	21	—	—	—	220	3.92
NIH 84-301 In house/C-NYD Evaluation of the NIH Small Business Innovative Research (SBIR) Program	84/10	89/12	D	—	—	80	80	200	360	3.94
NIH 84-302 In house Stability of Selected Biomedical Research Domains Among Institutes Over Time	84/02	86/01	D	33	46	11	—	—	90	3.96
NIH/DRG 84-301 In house Development of a Program Evaluation Information System of Grant Applicants, Trainees, and Fellows	84/07	66/10	D	3	20	17	—	—	40	3.97

Eval. Project No. Contract No. Project Title	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NIH/DRG 84-302 (263-84-C-0107) Comparison of Shortcomings in Clinical Basic and Behavioral Research Grant Applications	84/02	86/06	D	19	—	—	—	—	19	3.98
NIH/DRS 84-301 (N01-RS-6-2103) Evaluation of the Scientific Equipment Rental Program	85/11	86/10	D	—	—	95	—	—	95	3.99
NIH/DRS 84-303 (N01-RS-5-2119) Evaluation of the NIH Library Automated System	85/05	86/05	D	—	59	—	—	—	59	3.100
NIH/DRS 84-304 (263-84-C-0356) Short-Term Evaluation of the Veterinary Resources Branch	84/10	85/11	D	51	(17) 84	—	—	—	(17) 135	3.101
NIH/NLM 84-301 (N01-LM-4-3515) Evaluation of Medical Information Science (Medical Informatics)	85/01	86/03	D	125	—	—	—	—	125	3.102
NIH 85-301 In house Evaluation of the Utility of a Database Management System for a Program Information System	85/01	86/01	D	—	6	20	—	—	26	3.103
NIH 85-302 (N01-OD-5-2103) Evaluation of Sources of Research Training of U.S. Professors of Medicine	85/07	86/09	D	—	72	—	—	—	72	3.104

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NIH/NHLBI 85-303 Evaluation of Clinical Investigator Award (CIA): Design of a Follow-up Evaluation	In house	85/01	86/12	D	—	—	50	—	—	50	3.105
NIH/NICHD 85-304 Design and Development of Prototype Program Information System to Facilitate NIH BID Planning and Evaluation Functions	In house	85/04	86/09	D	—	36	59	—	—	95	3.106
NIH/NIDR 85-305 Evaluation of the NIDR Data Information Vocabularies	(263-85-C-0217)	85/10	86/09	D	—	71	—	—	—	71	3.107
NIH/NIDR 85-306 An Information System to Monitor the Performance of Thematic/Categorical Research Centers	(263-MD-5-35117)	85/09	86/03	D	—	9	—	—	—	9	3.108
NIH 85-308 Statistical Algorithm to Link NLM MESH and NIH CRISP Vocabularies into a Single Directory	In house	85/05	86/09	D	—	8	85	—	—	93	3.109
NIH/DRR 85-310 Evaluation of the Use of Animals in Research – Phase I (OASH/ASPE approval required for FY 1986 and FY 1987 funds)	Tr(ASU000001-04)	85/06	NYD	Under Review	—	135	200	295	—	630	3.37

Eval. Project No. Contract No. Project Title	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NIH 85-311 (N01-OD-5-2100) Survey of Academic Research Facilities: Status and Needs	84/11	86/09	D	—	159	134	—	—	293	3.110
NIH/NICHD 85-312 In house Matched Comparison Evaluation of NICHD Intramural Research Publications Using Biomedical Science Clusters	85/07	86/03	D	—	14	6	—	—	20	3.70
NIH 85-313 Tr(Y1-OD-5015) Assessment of the Effect of Modified Stratification on the Biomedical Research and Development Price Index	85/09	87/09	A	—	100	100	—	—	200	3.40
NIH/CC 85-314 In house Preliminary Assessment for a Study of Patient Classification System Alternatives in the NIH Clinical Center	85/08	86/09	D	—	4	21	—	—	25	3.74
NIH/DRG 85-315 In house Improvement of Information About Earned Degrees of Grant Applicants	85/09	86/09	D	—	—	50	—	—	50	3.78
NIH 85-316 Tr An Examination of Research Opportunities in Biology	85/09	87/08	D	—	—	167	—	—	167	3.44
NIH 86-301 In house Development of an Inventory of Data Elements in Existing Databases that are Useful for Program Evaluation	86/01	87/05	H	—	—	2	3	—	5	3.47

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NIH 86-302 Evaluation of the Applicability of Existing Artificial Intelligence (AI) Tools for the Improved Productivity of Biomedical Research Administration	In house	85/11	88/09	H	—	—	25	15	20	60	3.49
NIH/DRS 86-304 Productivity Evaluation of the Division of Research Services	C-NYD	86/08	88/07	A	—	—	225	150	100	475	3.9
NIH/NLM 86-305 Development of Evaluation Methodologies to Assess NLM's Coverage of New Biomedical Literatures	C-NYD	85/10	86/06	H	—	—	35	—	—	35	3.52
NIH/NLM 86-306 Evaluation of the Scope and Coverage of NLM's TOXLINE Database	C-NYD	86/01	87/09	H	—	—	75	30	—	105	3.55
NIH/DRR 86-307 Evaluation of NIH Shared Research Instrumentation Activities (Extramural)	C-NYD	86/05	87/10	B	—	—	300	—	—	300	3.16
NIH/NIDR 86-309 Assessment of NIH, Industry, and Academic Relationships in Restorative Materials Research	C-NYD	86/08	88/03	B	—	—	250	—	—	250	3.25
NIH/NIDR 86-310 Bibliometric Evaluation of Social and Behavioral Science Research in Dentistry	C-NYD	85/09	88/02	H	—	—	100	—	—	100	3.60

Eval. Project No. Project Title	Contract No.	Est./Actual Dates (Yr/Mo) Start	End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NIH/NCI 86-312 Evaluation of the Hospital and Clinical Research Project	Tr	85/09	86/08	D	—	190	—	—	—	190	3.30
NIH 86-313 A Comparative Analysis of Extramural Research Programs (not included in FY 1986 Plan)	C-NYD	86/06	88/08	Under Review	—	—	14	135	63	212	NA
NIH/DRR 86-314 An Examination of the Issues Surrounding the Use of Animals in Research - Phase II	C-NYD	NYD	NYD	Under Review	—	—	135	—	—	135	3.63
NIH 99-999 Evaluation Program Support Costs and Computer Services (not included in FY 1986 Plan)	In house	85/10	86/09	D	—	56	55	55	—	166	NA
RESERVE					—	—	182	—	—	182	
		NIH-Wide Total:			10,159	(206) 2,222	(232) 3,000	(212) 1,046	383	(650) 16,810	

Eval. Project No. Contract No. Project Title	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Cancer Institute										
NCI 80-304 In-house Evaluation of Cancer Communications Network (Phase I)	82/04	84/10	F	(60) 18	—	—	—	—	(60) 18	4.9
NCI 82-303 (N01-CM-2-7510) Cancer Therapy Evaluation Program (CTEP) Information System	82/08	86/09	D	(1,138) 270	(600) —	(228) —	—	—	(1,966) 270	4.10
NCI 83-301 (N01-CN-3-5009) Integrated Evaluation of Community Cancer Care Programs	83/09	86/08	D	(2,492) 1,296	—	—	—	—	(2,492) 1,296	4.12
NCI 83-304 (N01-CO-3-3933) An Assessment of the Factors Affecting Critical Cancer Research Findings	83/09	86/03	D	(71) 475	(100) —	—	—	—	(171) 475	4.5
NCI 83-305 (N01-CO-3-3851) Evaluation of NCI Mass Media Program: Television Public Service Announcements	84/07	86/02	D	35	—	—	—	—	35	4.14
NCI 84-401 (N01-CO-5-4059) Evaluation of NCI's Cancer Communications Program	84/04	87/03	D	—	(100) —	(281) —	(281) —	—	(662) —	4.15
NCI 84-402 C-NYD Development of the Cancer Control Tracking System	85/09	90/08	D	—	—	(250) —	(250) —	(750) —	(1,250) —	4.16

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NCI 84-403/405 Evaluation of the International Cancer Research Data Bank	C-NYD	85/08	87/03	D	—	(34) —	(125) —	(22) —	—	(181) —	4.17
NCI 85-401/402 PDQ User Groups and Vendors Evaluation	C-NYD	85/10	87/09	D	—	—	(237) —	(230) —	—	(467) —	4.18
		NCI Total:			(3,761) 2,094	(834) —	(1,121) —	(783) —	(750) —	(7,249) 2,094	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Eye Institute											
NEI 82-401 Design of a System for Evaluating the Implementation of the NEI 1983-87 Program Plan	In house	84/10	85/09	D	—	—	(50) —	—	—	(50) —	5.7
NEI 83-301 Evaluation of the NEI Small Grants Program	In house	82/11	85/10	D	2	—	—	—	—	2	5.9
NEI 86-401 Midcourse Evaluation of Third NEI Plan	In house	84/11	85/11	D	—	(24) —	(10) —	—	—	(34) —	5.5
		NEI Total:			2	(24) —	(60) —	—	—	(84) 2	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Heart, Lung and Blood Institute											
NHLBI 78-5 Evaluation of Progress in Pediatric Pulmonary Disease	In house	78/06	84/08	F	50	—	—	—	—	50	6.21
NHLBI 79-304 Evaluation of the Effect of Sickle Cell Counseling	(N01-HB-1-3006)	81/09	86/02	D	445	—	—	—	—	445	6.22
NHLBI 79-311 Evaluation of Regimen Compliance in Long-Term Clinical Trials	(N01-HV-5-2901)	79/06	84/09	F	155	—	—	—	—	155	6.23
NHLBI 80-304 Evaluation of Statewide Hypertension Programs	(N01-HO-3-7007)	80/06	86/09	D	346	(258) —	—	—	—	(258) 346	6.25
NHLBI 80-310 Assessment of Reach and Frequency of High Blood Pressure Messages	(263-82-C-0021)	81/09	87/09	D	145	(45) —	(45) —	(45) —	—	(135) 145	6.26
NHLBI 81-313 Evaluation of the Framingham & Other CHD Risk Models in a Large National Cohort	Tr(Y01-HV-10047)	81/05	84/06	F	100	—	—	—	—	100	6.28
NHLBI 82-308 Evaluation of a Demonstration Program for Hypertension Control Using Community Health Centers (Phase II: Conduct of the Evaluation)	(N01-HC-2-8003)	82/02	86/12	D	256	(153) —	—	—	—	(153) 256	6.29

Eval. Project No. Contract No. Project Title	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NHLBI 83-403 (NO1-HB-4-7000) Assessment of the Collection, Processing, and Use of Blood Resources	84/06	85/07	E	(50)	—	—	—	—	(50)	6.30
NHLBI 83-405 (NO1-HV-4-8074) Evaluability Assessment of the Minority Hypertension Research Development Summer Program	84/06	85/12	D	(130)	—	—	—	—	(130)	6.31
NHLBI 84-402 Tr(1YO1HV40047) Evaluation of the Framingham and Other CHD Risk Models in a Large National Cohort: Phase II—Supplementary Data Collection and Analysis	84/03	85/09	D	(150)	—	—	—	—	(150)	6.33
NHLBI 84-404 (NO1-HC-4-8075) Programmatic Evaluation of Biobehavioral Approaches to Treatment of Hypertension	84/02	86/07	D	(130)	(110)	(150)	—	—	(390)	6.34
NHLBI 84-405 (NO1-HV-5-8082) Evaluation of Impact of the Coronary Primary Prevention Trial and Multiple Risk Factor Intervention Trial: Measurement of Practice After Release of Clinical Trial Results	85/10	86/01	D	—	(200)	—	—	—	(200)	6.36

	Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Contract No. Project Title	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NHLBI 84-406 Tr (Y01-HV-40007 & Y01-HV-50044) Evaluation of the Impact of the Coronary Primary Prevention Trial on Public Attitudes, Knowledge and Behavior Regarding Serum Cholesterol and Other Risk Factors for Coronary Heart Disease	84/01	85/09	D	(75)	(84)	—	—	—	(159)	6.37
NHLBI 85-401 (N01-HR-5-6025) Survey of Physician Practice Behaviors Related to the Prevention of Lung Disease	85/09	87/09	D	—	(198)	—	—	—	(198)	6.39
NHLBI 85-402 In house Assessment of the Role and Impact of Specialized Centers of Research	85/03	87/09	A	—	—	(50)	—	—	(50)	6.40
NHLBI 85-403 (N01-HB-5-7006) Transfusion Medicine Academic Award Program Evaluation	84/11	90/11	D	—	(51)	(48)	(51)	(85)	(235)	6.42
NHLBI 85-404 In house Analysis of Antihypertensive Drug Prescriptions	85/07	85/10	D	—	(1)	—	—	—	(1)	6.43
NHLBI 85-405 (N01-HO-5-9000) High Blood Pressure: 1986 Survey of Physicians' Knowledge, Attitudes, and Reported Behavior	85/09	87/12	D	—	(74)	(251)	—	—	(325)	6.44

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NHLBI 86-401 Coronary Heart Disease Risk Factors in Children: Current Physician Attitudes, Knowledge, and Practice	C-NYD	86/03	89/02	B	—	—	(50) —	(150) —	(100) —	(300) —	6.5
NHLBI 86-402 Knowledge, Attitudes, and Behavior of Nurses and Dietitians Regarding Cardiovascular Risk Factors	C-NYD	86/06	88/08	B	—	—	(75) —	(200) —	(75) —	(350) —	6.8
NHLBI 86-403 Evaluation of the Use of Nutrition Counseling Skills Publications (not included in FY 1986 Plan)				G	—	—	—	—	—	—	6.11
NHLBI 86-404 Public Attitudes and Practice Regarding Cholesterol and Coronary Heart Disease	C-NYD	86/09	87/08	H	—	—	(89) —	—	—	(89) —	6.14
NHLBI 86-405 Evaluation of Pulmonary Faculty Development Award	C-NYD	85/10	86/06	H	—	—	(30) —	—	—	(30) —	6.17
	NHLBI Total:				(535) 1,597	(1,174) —	(788) —	(446) —	(260) —	(3,203) 1,597	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute on Aging											
NIA 83-301 Evaluation of the Research Program in Alzheimer Disease - Component 1 (Effectiveness Study)	(263-84-C-0287)	84/06	86/09	D	75	—	(33) —	—	—	(33) 75	7.5
NIA 83-301 Evaluation of the Research Program in Alzheimer Disease - Component 2 (Social/Economic Cost Study)	(N01-HE-3-2123)	83/09	84/09	E	74	—	—	—	—	74	7.6
NIA 85-401 Evaluation of Research Training and Career Development Programs in Gerontology and Geriatrics	C-NYD	85/06	86/11	D	—	—	(NYD) —	—	—	0 —	7.7
		NIA Total:			149	—	(33) —	—	—	(33) 149	

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases											
NIADDK 85-401 Study of Obesity Research Awards	In house	85/08	85/12	D	—	(2)	(3)	—	—	(5)	8.5
		NIADDK Total:			—	(2)	(3)	—	—	(5)	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of Allergy and Infectious Diseases											
NIAID 82-301 Evaluation of Decision Analysis Model Systems for the Accelerated Development of New Vaccines Program	(N01-AI-2-2678)	82/09	85/06	D	481	—	—	—	—	481	9.5
		NIAID Total:			481	—	—	—	—	481	

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of Child Health and Human Development											
NICHD 82-302 Stage 2 Evaluation of NICHD Child and Adolescent Development Research Program	In house	82/09	84/12	E	20	—	—	—	—	20	10.11
NICHD 82-304 Stage 2 Evaluation of NICHD Mental Retardation Research Program	In house	82/09	86/03	D	—	—	—	—	—	—	10.12
NICHD 84-401 Evaluation of Contraceptive Development Program	In house	84/01	85/12	D	(4)	(2)	—	—	—	(6)	10.13
NICHD 84-402 Evaluation of Contraceptive Evaluation Program	In house	84/01	85/12	D	(1)	(1)	—	—	—	(22)	10.14
NICHD 84-404 Update of NICHD Physiological Development and Endocrinology Research Plan	In house	84/04	85/06	F	(22)	—	—	—	—	(22)	10.15
NICHD 84-405 Evaluation of Addition of Interviews to the Peer Review of Physician Scientist and Clinical Investigator Applications	In house	84/07	86/02	D	(2)	(5)	(10)	—	—	(7)	10.16

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NICHD 85-401 Impact Evaluation of Cesarean Childbirth Consensus Conference	In house	84/10	86/02	D	—	(34)	—	—	—	(34)	10.17
NICHD 85-402 Update of NICHD Congenital Defects Program Research Plan	In house	84/10	86/06	D	—	—	(22)	—	—	(22)	10.18
NICHD 85-403 Update of NICHD Nutrition Program Research Plan (not included in FY1986 Plan)	In house	NYD	NYD	C	—	—	—	(22)	—	(22)	
NICHD 85-404 Update of NICHD Pregnancy, Birth, and the Infant Program Research Plan	In house	85/10	86/09	C	—	—	(25)	—	—	(25)	10.5
NICHD 85-405 Update of NICHD Fertility and Infertility Program Research Plan (not included in FY1986 Plan)	In house	NYD	NYD	C	—	—	—	(22)	—	(22)	
NICHD 85-406 Update of NICHD Demographic and Behavioral Sciences Program Research Plan	In house	85/10	86/12	C	—	—	(22)	—	—	(22)	10.7

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NICHD 86-01 Impact Evaluation of Grants Process Orientation for Pediatric Scientist Training Program	In house	85/10	86/01	K	—	—	(5) —	—	—	(5) —	10.9
		NICHD Total:			(29) 20	(42) ---	(84) ---	(44) ---	—	(195) 20	

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of Dental Research											
NIDR 83-301 Evaluation of Selected Oral Health Education and Promotion Activities of the National Caries Program	(N01-DE-3-2445)	83/09	86/01	D	93	—	—	—	—	93	11.5
NIDR 83-302 Assessment of the Effectiveness of NIDR Training Programs in Preparing Dental Clinical Investigators	(N01-OD-1-2109)	83/06	85/11	D	—	—	—	—	—	—	11.6
NIDR 85-401 NIDR Long-Range Research Plan: Creation of a Database and a Monitoring/Implementation Process	In house	84/07	85/10	D	—	(10) —	—	—	—	(10) —	11.7
		NIDR Total:			93	(10) —	—	—	—	(10) 93	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of Environmental Health Sciences											
NIEHS 83-401 Manpower in the Field of Environmental Epidemiology Evaluation and Survey	(N01-ES-4-5049)	84/09	87/03	D	(76)	(165)	—	—	—	(241)	12.5
NIEHS 84-401 Third Task Force on Research Planning in Environmental Health Science	Tr	83/09	85/06	D	(432)	(70)	—	—	—	(502)	12.7
NIEHS 84-402 Panel on Chemical Carcinogenesis Testing and Evaluation	In house	83/05	84/08	E	(130)	—	—	—	—	(130)	12.9
NIEHS 84-403 Manpower in the Field of Environmental Toxicology-Evaluation and Survey	(N01-ES-4-5074)	84/09	87/03	D	(66)	(185)	—	—	—	(251)	12.11
NIEHS 84-404 NIEHS Program Analysis System	Tr	84/04	89/12	D	(50)	—	(292)	(270)	—	(612)	12.13
		NIEHS Total:			(754)	(420)	(292)	(270)	—	(1,736)	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of General Medical Sciences											
NIGMS 82-401 Evaluation of Shared Instrumentation Initiative	In house	81/09	86/01	D	(8)	—	—	—	—	(8)	13.9
NIGMS 86-401 Evaluation of GenBank—The Genetic Sequence Data Bank	C-NYD	86/01	86/12	K	—	—	(20)	(10)	—	(30)	13.5
		NIGMS Total:			(8)	—	(20)	(10)	—	(38)	

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Institute of Neurological and Communicative Disorders and Stroke											
NINCDS 82-302 Survey of Practice in the Management of Febrile Seizures	In house	82/06	85/05	E	43	(10) —	—	—	—	(10) 43	14.23
NINCDS 83-301 Survey of Antiepileptic Drug Usage	(N01-NS-3-2354)	83/09	84/08	E	114	—	—	—	—	114	14.25
NINCDS 85-401 Assessment of New Directions in ALS Research	In house	84/06	85/03	F	—	(10) —	—	—	—	(10) —	14.17
NINCDS 85-402 Review of Research in Developmental Neurobiology (Two Projects)	In house	84/06	85/10	D	—	(16) —	—	—	—	(16) —	14.17
NINCDS 85-403 Analysis of Research Re: The Prevalence of LAV Virus Antibodies in AIDS and Pre-AIDS Patients	In house	84/06	84/10	F	—	—	—	—	—	—	14.17
NINCDS 85-404 International Review of Research in Auditory Biochemistry	In house	84/06	85/12	F	(21) —	(14) —	—	—	—	(35) —	14.18
NINCDS 85-406 Head Injury Research Evaluation	In house	84/06	85/12	F	—	(58) —	—	—	—	(58) —	14.18

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NINCDS 85-407 Stroke Research Evaluation	In house	84/06	85/12	F	—	(58)	—	—	—	(58)	14.18
NINCDS 85-409 Assessment of Need for Naturally-Occurring Animal Models of Human Neurological Disease	In house	84/06	85/01	F	—	(6)	—	—	—	(6)	14.19
NINCDS 85-410 Assessment of Neural Prostheses	In house	84/06	85/12	D	—	(12)	(12)	(12)	—	(36)	14.19
NINCDS 85-411 Assessment of Molecular Biology of Lysosomal Storage Disorders	In house	85/10	86/06	C	—	—	(10)	—	—	(10)	14.19
NINCDS 85-412 Assessment of Intensive Monitoring of Epileptic Seizures	In house	85/10	86/03	C	—	—	(21)	—	—	(21)	14.20
NINCDS 85-413 Review and Analysis of Neuroimmunomodulation	In house	84/06	85/03	F	—	(20)	—	—	—	(20)	14.20
NINCDS 85-414 Assessment of Research in Otolaryngology	In house	85/09	86/03	D	—	(20)	—	—	—	(20)	14.20
NINCDS 85-415 Review of Impact of Neurobiology Research on Neurosurgery	In house	84/06	86/12	D	—	(25)	—	—	—	(25)	14.21

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NINCDS 86-401 Analysis of the Development of Social Cognition, Normal and Disordered, in Relation to the Diagnosis of Autistic Disorder	In house	85/10	86/09	K	—	—	(10) —	—	—	(10) —	14.11
NINCDS 86-402 Evaluation of Protocol Design for Clinical Testing of Antiepileptic Drugs	In house	85/10	86/09	K	—	—	(10) —	—	—	(10) —	14.11
NINCDS 86-403 Examination of Research on Chemical Reception and Chemical Irritants	In house	85/10	87/09	K	—	—	(20) —	—	—	(20) —	14.12
NINCDS 86-404 Review of Research on Presbycusis	In house	85/10	86/09	K	—	—	—	—	—	—	14.12
NINCDS 86-405 Assessment of Studies Related to Development of Cochlear Implants	In house	85/10	87/09	K	—	(8) —	—	—	—	(8) —	14.12
NINCDS 86-406 Assessment of Studies Related to Development of Communicative Devices for Non-Vocal Patients	In house	85/10	87/09	K	—	—	—	—	—	—	14.12
NINCDS 86-407 Assessment of Communicative Prostheses for Pre-Lingual Deaf Children	In house	85/06	85/12	K	—	(15) —	—	—	—	(15) —	14.13

Eval. Project No. Contract No. Project Title	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NINCDS 86-408 C-NYD Critical Review of Case-Control Studies of Risk Factors for Hearing and Tinnitus	85/06	88/06	K	—	—	(50) —	(50) —	—	(100) —	14.13
NINCDS 86-409 In house Review of Studies on the Auditory Effects of Noise Publication	85/06	85/10	K	—	(15) —	—	—	—	(15) —	14.14
NINCDS 86-410 In house Assessment of Studies on Multiple Sclerosis	85/06	85/12	K	—	(88) —	—	—	—	(88) —	14.14
NINCDS 86-411 In house International Review of the Use of Neural Prostheses for Motor Control	85/06	85/12	K	—	(15) —	—	—	—	(15) —	14.14
NINCDS 86-412 In house Assessment of Brain Tumor Research and Therapy	85/06	85/12	K	—	—	(24) —	—	—	(24) —	14.14
NINCDS 86-413 In house Review of Neurobehavioral Recovery from Head Injury	85/06	85/12	K	—	(26) —	—	—	—	(26) —	14.15
NINCDS 86-414 In house Review of Clinical Trials in MS	85/06	85/12	K	—	—	(4) —	—	—	(4) —	14.15
	NINCDS Total:			(21) 157	(416) —	(161) —	(62) —	—	(660) 157	

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
Division of Research Resources											
DRR 80-401 Major Clinical Applications of Research Findings Accomplished at General Clinical Research Centers	In house	79/11	NYD	D	---	---	---	---	---	---	16.5
DRR 84-401 Evaluation of the Activities of the Biotechnology Resources Program in the Area of Mass Spectrometry	In house	84/03	84/07	F	---	---	---	---	---	---	16.6
DRR 85-401 Evaluation of the Need for Supercomputer Access	In house	84/03	84/12	E	---	---	---	---	---	---	16.7
DRR 85-402 Evaluation of the Biotechnology Resources Small Grant Program	In house	84/04	84/12	E	---	---	---	---	---	---	16.8
DRR 85-403 Outcome Study of the Clinical Associate Physician Program	In house	85/03	86/NYD	D	---	---	---	---	---	---	16.9
		DRR Total:			---	---	---	---	---	---	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
National Library of Medicine											
NLM 80-401 Evaluation of Medical Library Resource Project Grant Program	In house	79/11	NYD	D	(24)	---	---	---	---	(24)	15.9
NLM 80-402 Consultant Review of Lister Hill Center Programs	In house	79/10	NYD	D	(10)	(10)	(10)	(10)	---	(40)	15.10
NLM 80-404 Medical Library Assistance Act Program Performance Evaluations	In house	76/10	NYD	D	(56)	---	(8)	---	---	(64)	15.11
NLM 82-303 Study of Audiovisual Selection-Acquisition Process	(N01-LM-2-3511)	82/07	85/05	E	141	---	---	---	---	141	15.12
NLM 83-401 Assessment of CHEMLINE	In house	84/06	85/12	D	---	(15)	---	---	---	(15)	15.13
NLM 84-401 Evaluation of HISTLINE Database	In house	84/01	85/04	F	(5)	(5)	---	---	---	(10)	15.14
NLM 84-402 Analysis of Inter-library Loan Requests for Serial Services	In house	84/01	85/09	F	(5)	(5)	---	---	---	(10)	15.15

		Est./Actual			SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( )						
Eval. Project No. Project Title	Contract No.	Dates Start	(Yr/Mo) End	Status Code	Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
NLM 86-401 Field Test and Evaluation of the MEDLINE Optical Disk (MOD) System	C-NYD	86/02	86/09	H	—	—	(75) —	—	—	(75) —	15.5
		NLM Total:			(100) 141	(35) —	(93) —	(10) —	—	(238) 141	

Eval. Project No. Project Title	Contract No.	Est./Actual Dates Start	(Yr/Mo) End	Status Code	SET-ASIDE FUND EXPENDITURES $ IN THOUSANDS Institute Funds in ( ) Prior Years	FY 85	FY 86	FY 87	Future Years	PROJECT TOTAL	PAGE NO.
Fogarty International Center											
FIC 82-301 Evaluation of Senior International Fellowship Program (SIFP)	(N01-TW-3-2109)	83/05	85/12	D	158	—	—	—	—	158	17.5
FIC 85-401 Assessment of Scientific and Professional Accomplishments of Former International Research Fellows	C-NYD	85/12	87/12	D	—	—	(150) —	—	—	(150) —	17.6
		FIC Total:			158	—	(150) —	—	—	(150) 158	

3

OFFICE OF THE DIRECTOR, NIH

James B. Wyngaarden, Director

Contents

List of Projects and Proposed Budget 3.3

New and Continuing Set-Aside Proposals Over $135,000 3.9

New and Continuing Set-Aside Proposals $135,000 and Under 3.47

Evaluation Documentation Center Forms for Continuing and Recently Completed Projects 3.81

Office of the Director: Proposed Budget

		$ in Thousands		
		FY 85	FY 86	FY 87
NIH 75-1	NAS Continuing Study of National Needs for Biomedical and Behavioral Research Personnel	581 (64)	497 (75)	495 (80)
NIH 81-302	Evaluation of Present Strategy for Dissemination of Consensus Development Statements and of the Impact of the Consensus Development Program on the Practice of Medicine (Impact Study)	7	---	---
NIH 82-302	Evaluation of Research Manpower and Training Evaluation Activities	64	10	---
NIH 83-301	Evaluation of Biomedical Research Publication Performance	315 * (125)	--- (157)	--- (132)
NIH 83-302	An Evaluation of the Impact of RCDAs on the Receipients of The Awards	165	---	---
NIH 84-301	Evaluation of the NIH Small Business Innovative Research (SBIR) Program	---	80	80
NIH 84-302	Stability of Selected Biomedical Research Domains Among Institutes Over Time	46	11	---
NIH/DRG 84-301	Development of a Program Evaluation Information System of Grant Applicants, Trainees, and Fellows	20	17	---

* Includes funding for both FY 85 and FY 86, plus 100 added by NIMH

		$ in Thousands FY 85	 FY 86	 FY 87
NIH/DRG 84-302	Comparison of Shortcomings in Clinical Basic and Behavioral Research Grant Applications	---	---	---
NIH/DRS 84-301	Evaluation of the Scientific Equipment Rental Program	---	95	---
NIH/DRS 84-303	Evaluation of the NIH Library	59	---	---
NIH/DRS 84-304	Short-Term Evaluation of the Veterinary Resources Branch	84 (17)	---	---
NIH/NLM 84-301	Evaluation of Medical Information Science (Medical Informatics)	---	---	---
NIH 85-301	Evaluation of the Utility of a Database Management System for a Program Information System	6	20	---
NIH 85-302	Evaluation of Sources of Research Training of U.S. Professors of Medicine	72	---	---
NIH/NHLBI 85-303	Evaluation of Clinical Investigator Award (CIA): Design of a Follow-up Evaluation	---	50	---
NIH/NICHD 85-304	Design and Development of Prototype Program Information System to Facilitate NIH BID Planning and Evaluation Functions	36	59	---

		$ in Thousands		
		FY 85	FY 86	FY 87
NIH/NIDR 85-305	Evaluation of the NIDR Data Information Vocabularies	71	---	---
NIH/NIDR 85-306	An Information System to Monitor the Performance of Thematic/Categorical Research Centers	9	---	---
NIH 85-308	Statistical Algorithm to Link NLM MESH and NIH CRISP Vocabularies into a Single Directory	8	85	---
NIH/DRR 85-310	Evaluation of the Use of Animals in Research - Phase I	135	200 *	295 *
NIH 85-311	Survey of Academic Research Facilities: Status and Needs	159	134 **	---
NIH/NICHD 85-312	Matched Comparison Evaluation of NICHD Intramural Research Publications Using Biomedical Science Clusters	14	6	---
NIH 85-313	Assessment of the Effect of Modified Stratification on the Biomedical Research and Development Price Index	100	100	---

* 135 initially approved by NIH for pilot study. Funds needed for full-scale national survey will require DASH/ASPE review.

** 200 previously approved; however, should OMB approve survey questionnaire the contract total will be 273 (obligated 111 to date). Additional 20 has been obligated for two professional services contracts at beginning of project.

		$ in Thousands		
		FY 85	FY 86	FY 87
NIH/CC 85-314	Preliminary Assessment for a Study of Patient Classification System Alternatives in the NIH Clinical Center	4	21	---
NIH/DRG 85-315	Improvement of Information About Earned Degrees of Grant Applicants	---	50	---
NIH 85-316	An Examination of Research Opportunities in Biology	---	167	---
NIH 86-301	Development of an Inventory of Data Elements in Existing Databases that are Useful for Program Evaluation	---	2	3
NIH 86-302	Evaluation of the Applicability of Existing Artificial Intelligence (AI) Tools for the Improved Productivity of Biomedical Research Administration	---	25	15
NIH/DRS 86-304	Productivity Evaluation of the Division of Research Services	---	225	150
NIH/NLM 86-305	Development of Evaluation Methodologies to Assess NLM's Coverage of New Biomedical Literatures	---	35	---
NIH/NLM 86-306	Evaluation of the Scope and Coverage of NLM's TOXLINE Database	---	75	30
NIH/DRR 86-307	Evaluation of NIH Shared Research Instrumentation Activities (Extramural)	---	300	---

		$ in Thousands		
		FY 85	FY 86	FY 87
NIH/NIDR 86-309	Assessment of NIH, Industry, and Academic Relationships in Restorative Materials Research	---	250	---
NIH/NIDR 86-310	Bibliometric Evaluation of Social and Behavioral Science Research in Dentistry	---	100	---
NIH/NCI 86-312	Evaluation of the Hospital Cost and Clinical Research Project	190	---	---
NIH 86-313	A Comparative Analysis of Extramural Research Programs	---	14 *	135 *
NIH 86-314	An Examination of the Issues Surrounding the Use of Animals in Research - Phase II	---	135 *	---
NIH 99-999	Evaluation Program Support Costs and Computer Services	56	55	55
	RESERVE		182	

Total FY 86 Set-Aside Fund Request			3,000 (232)	

Reviewed and approved by
NIH Committees

1. Project ID# and Agency Proposing:

NIH/DRS 86-304

2. Project Title and Capsule Description

a. Title: Productivity Evaluation

b. Capsule Description: Activities in the Division of Research Services which cut across NIH organizational lines will be reviewed and evaluated to examine the plans and objectives, organizational structure, policies, systems, procedures, methods of control, facilities, standards of performance and the measurement of results. Areas of evaluation include the Office of the Director, Biomedical Engineering and Instrumentation Branch, NIH Library, Medical Arts and Photography Branch and Veterinary Resources Branch.

3. Cost and Funding Source:

Fiscal Year	Program	Expenditure
86	Biomedical Engineering and Instrumentation Branch o Mechanical Instrument and Fabrication Section o Research Instrumentation Section o Clinical Care and Instrumentation Section o Material and Clerical Operations Section	$100,000
86	NIH Library	$125,000
87	Biomedical Engineering and Instrumentation Branch o Mechanical, Electrical and Electronic, Chemical and Applied Clinical Engineering Sections	$70,000
87	Medical Arts and Photography Branch	$80,000
88	Veterinary Resources Branch	$100,000

Justification:

The cost estimate of these studies is based on experience with other contractors performing similar studies.

This study cannot be completed in house because DRS does not have the staff to complete studies of this magnitude. Further, while it is acknowledged that there will be significant input from DRS staff in the completion of this effort, the actual performance of the studies must be performed by an objective non-government expert. This would help to ensure the performances of unbiased studies which would contain valid information for making the required resource decisions.

4. Project Monitor/Contact:

Cherie Nichols/
Robert Weymouth
Management Analysis Office
Division of Research Services
Room 4051 Building 12A
(301) 496-4501

5. Coordination:

DRS Review:

Dr. Robert Whitney, Acting Director
Mr. John Smart, Executive Officer
Ms. Jane Leitch, Budget Officer
Branch Chiefs and Administrative Officers as applicable

6. Program Evaluated:

The Division of Research Services is structured to provide products and services in support of the sequential steps in every biomedical research project: planning, making available models and substrates, manipulating and measuring research materials, and recording and communicating research results.

- The Library Branch possesses or has access to virtually all published biomedical knowledge and has staff expertise to assist investigators in planning and designing their projects.

- The Veterinary Resources staff consults and collaborates with investigators in providing the animal models, organic materials, and proper facilities for their use.

- The Biomedical Engineering and Instrumentation staff collaborates with investigators in devising the means whereby unique research materials may be fabricated and manipulated and the results measured, often with highly sophisticated electronic equipment.

- o The skills of the Medical Arts and Photography staff are available to all investigators to enable them to record and communicate the results of their research to the scientific community.

7. Intended Users:

a. Primary Users:

Director, DRS
Executive Officer, DRS
Budget Officer, DRS
Management Analysis Officer, DRS
Branch Chiefs (as applicable), DRS

Findings of this evaluation are needed to access the current status of DRS Programs to identify areas which potentially could be improved. A formal evaluation has never been performed on most DRS programs to ensure they are adequately meeting the needs of the NIH research community. Such evaluations are critical in order for the DRS programs to continue their support of the research community, in light of the severe budget constraints and cutbacks of FTEs.

The Division is currently embarking on a 12% FTE reduction program to be accomplished over the next three years. These savings will be realized by curtailing some activities while improving in-house staff efficiency and productivity. Additional FTE savings may be realized through these evaluation studies which will provide DRS and NIH management with comparable program performance information on all major DRS programs for use in planning and resource allocation, while maintaining the Divisions committment to quality.

Such an evaluation becomes critical in order for DRS to be apprised of both perception and user satisfaction, and especially to address prescribed productivity improvement and/or cost reduction initiatives.

These evaluations will provide DRS management with performance information on the above services and where warranted, new directions. Of particular interest are timeliness, quality and costs.

Time Table

Program	RFP Developed	Evaluation Begun	Final Report
BEIB-fabrication, maintenance, and clerical	August 1985	February 1986	September 1986
NIH Library	September 1985	March 1986	October 1986
BEIB-professional engineers	April 1986	October 1986	April 1987
MAPB	October 1986	April 1987	October 1987
VRB	April 1987	October 1987	July 1988

It is anticipated each program review will take approximately six months.

8. Information to be Generated

The quality of any support organization is directly dependent upon its ability to satisfy its customers. DRS' primary goal must be to provide our customers with the best and most up-to-date services possible. The Division continually assesses user needs through heavy reliance on our user committees, direct DRS staff contact with investigators as services are rendered, and our extensive collaborative research program.

In addition to these ongoing assessments, major evaluation projects, conducted by contractors using the one percent evaluation set-aside funds, will give in-depth analysis of some of our most important services to the NIH intramural community. The evaluations will also focus on comprehensive in-house user and non-user surveys to determine the level of satisfaction with a number of important current services and needs for any new products and services. The Division focus must continually be on how the programs satisfy our customers by improving our current products and services or developing innovative methods for providing the resources required to conduct biomedical research at NIH effectively.

Each program within DRS would be reviewed to assess areas of concern such as:

(1) Whether the current organization structure is responsive to its intended goals.

(2) Whether the program is responsive to the investigator or other target units to which it is addressed.

(3) Whether the program is providing an expeditious and efficient response.

(4) Whether the program is cost-effective in its operations.

(5) Whether the program can increase or expand its customer base by penetrating new markets.

(6) Whether or not consolidation of production activities can be effected to increase space for expanding or new services.

(7) Whether the introduction of technologic improvements in production facilities or in administrative data flow will result in cost reductions.

(8) Whether the work of a particular employee providing some some service can be traced expeditiously and objectively.

(9) Whether professional staff involvement in the discussion of work done by the programs can improve the quality of products, and whether such involvement should be provided routinely in a formal setting.

9. Approach:

A. General

The contractor will identify performance indicators to apply to each program area and develop criteria for selecting activities where further comprehensive review is likely to benefit. The approach proposed will consist of short-term evaluations of all programs referenced. Specifically, the contractor will (1) review and develop information describing the programs, develop objectives specifying performance indicators, and identify major program problems and issues, and (2) describe long-term full scale evaluations of the programs that could be undertaken, specifying the information that would result, the probable cost and duration, and the likelihood of success and utility.

DRS staff will provide the contractor with background information. In addition to interviews with program staff and branch management, the contractor will develop questionnaires to survey both the administrative and research community to determine what method BIDs use to acquire both commercial and DRS products and services. Further, they would be asked to give reasons why they use other services instead of DRS and which method they prefer to use.

The contractor would be asked to perform a cost analysis of a random sampling of products and services acquired through DRS. This would be compared to a similar cost analysis of a random sampling of products and services ordered through the internal BID procurement process to determine the most cost effective methods.

In addition to the cost analysis, the contractor will survey the same user group to determine the level of satisfaction with current DRS programs and to determine the need for additional support. Once the surveys are complete, the contractor will review each DRS program and attempt to answer as many of the questions listed in the previous section in order to determine in general, the program's effectiveness and efficiency.

B. Specific

I. Planning Stage

- A. Scope/Boundaries
- B. Define Objectives
  - 1. develop optimum organizational structure
  - 2. document specific management improvements
- C. Create Study Team
- D. Draft memo to organization being studied
- E. Identify constraints and way to compensate
  - 1. management policy
  - 2. legal
  - 3. fiscal
  - 4. equipment and facilities
- F. Define assumptions (ie. workload remains fixed over a defined period of time)

- G. Prepare study approach
  - 1. define information to be gathered
  - 2. methodologies to be used
  - 3. documentation to be produced
  - 4. generation of required reports
  - 5. assignment of tasks to team members
  - 6. creation of milestone chart
- H. Acquire necessary approval(s)

II. Preparation Stage

- A. Identify potential information sources
- B. Develop data collection forms and questionnaires
- C. Develop interview schedule

III. Data Definition, Collection, and Design Stage

- A. Determine products and/or services the organization provides.
- B. Identify tasks that comprise each service
- C. Ascertain resources required to undertake identified tasks
- D. Define the Workload
  - 1. Specify standard of acceptable quality levels (AQL)

IV. Establish Efficiency of Present Operations

- A. Historical Data
- B. Self Logging
- C. Simple Timing (observation)
- D. Work Sampling
- E. Time Study
- F. Non-random sampling
- G. Predetermined time standards

V. Organizational/Operations Analysis

- A. Work distribution analysis
- B. Work flow analysis

VI. Develop and Document Recommendations involving

- A. Restructure the organization
- B. Change the current procedures
- C. Reconfiguration of work environment
- D. Modification equipment configuration
- E. Eliminate or downgrade positions

VII. Write Interim Reports and Give Briefings
Write Management Study Report

VIII. Brief Management On Findings of Management Study Report

IX. Finalize Report - Time Schedule of Changes

X. Document Management Study - Audit Trail

- A. Source documents
- B. Workload data
- C. Findings
- D. Assumptions made and rationale
- E. Requests for management decisions and results of requests
- F. Conclusions

10. Information Clearance/Collection:
None.

11. Pre-Rule Making Activity: No

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier: NIH/DRR 86-307

2. Project Title and Capsule Description:

   a. Title: Evaluation of NIH Shared Research Instrumentation Activities (Extramural)

   b. Capsule Description: A questionnaire survey will be used to evaluate the implementation and impact of the DRR and NIGMS Shared Instrumentation Grant Programs

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Changes (in thousands)	Other Expenditures (in thousands)
86	$ 300	--	--
87	--	--	--

Justification

NIH does not have sufficient staff time to accomplish this study by itself. NIH staff will oversee the project and work closely with the contractor during the development of the survey instruments. A contractor expert in program evaluation, as well as survey design, operation and analysis--with advice and assistance from NIH staff and non-NIH scientists knowledgeable about instrumentation--will develop and perfect the survey forms; design a sample selection procedure; conduct the mail survey and necessary follow-up; reduce and analyze the survey data; and, produce a final report using the survey data, data from other studies (e.g. NIH 83-311, Evaluation of Biomedical Research Instrumentaton in the U.S.); and, data from grant applications, progress reports, grant files, IMPAC, CRISP, etc.

The cost estimate is based on the cost of similar studies, and reflects the professional judgments of NIH evaluation staff and project officers of comparable contracts. This survey will be unusually complex because it must deal with at least fourteen categories of instruments, five major types of grantee institutions, and sites serving both small (3-9 persons) and large (10-20 persons) groups of users. Information may need to be obtained from principal investigators; from technical experts at grantee institutions (where present) responsible for the operation/maintenance of the instruments; from PHS-supported users; from individuals involved with local committees that advise grantees regarding the sharing and operation of the instruments; and from other institutional officials.

4. Project Monitor/Contact: Martin B. Blumsack, Evaluation Officer, Office of Program Planning and Evaluation, Division of Research Resources,

National Institutes of Health, Building 31, Room 5B54, Bethesda, Maryland 20205, FTS 496-5507 or (301) 496-5507.

5. Coordination: This project will be reviewed by the NIH Evaluation Policy and Oversight Committee, and the NIH Technical Review Committee. It has already been reviewed by the staff of the Shared Instrumentation Program, DRR, and the Shared Instrumentation Program, NIGMS, as well as the Offices of the Directors of DRR and NIGMS. Primary coordination during the course of this project will be the responsibility of:

Dr. Marjorie A. Tingle, Chief
Biomedical Research Support
Shared Instrumentation Grant
Activity, DRR
Building 31, Room 5B23
Bethesda, MD 20205
(301) 496-6743

Dr. Marvin Cassman, Director
Biophysics and Physiological
Sciences Program, NIGMS
Westwood Bldg., Room 909
Bethesda, MD 20205
(301) 496-7463

6. Program Evaluated:

PHS-NIH-Biomedical Research
PHS-NIH-Biomedical Research - Research Resources
PHS-NIH-Biomedical Research - Institute Specific - General Medical Sciences
PHS-NIH-Biomedical Research Activity - Research Grants and Contracts
PHS-NIH-Biomedical Research Activity - Program Direction and Management

The objective of these programs is to make available, to institutions, major research instrumentation on a shared-use basis for groups of PHS-funded investigators (see Table 1). The NIH shared instrumentation programs have, since 1979, made competitive awards totaling $80 million (see Table 2) for 509 instruments.

The NIH Shared Instrumentation Grants can be used to support any kind of instrumentation or equipment provided that each item or system requested has a cost of at least $30,000, in the case of NIGMS, or $100,000 for the DRR program. There is no upper limit to the cost of instrumentation that can be requested, but the maximum contribution in the equipment category is $200,000 from NIGMS or $300,000 from DRR for any one award. If the amount of funds requested does not cover the total cost of the instrument, an award is made only when the remainder of the funding is assured by the applicant institution.

DRR grants are awarded for a period of one year, are not renewable, and supplemental applications are not accepted. The institution must meet costs required to place the instrumentation in operational order as well as the maintenance, support personnel and service costs associated with maximum utilization.

NIGMS grants are awarded for a period of up to three years and are not renewable. Support for maintenance of the instruments may be requested for the period of the grant, along with part of the salary of a qualified technician. Provisions for continued maintenance of the equipment and for technical support beyond the period of the grant must be made by the applicant.

The principal investigator on an application for a NIGMS Shared Instrumentation Grant must hold an active NIGMS research grant. In addition, there must be a clear need for the instrumentation by the projects supported by NIGMS research grants and these projects must use the instrumentation for a substantial portion of the available time. A major user group of three or more investigators (including the principal investigator) must be identified who will use the equipment at least 75% of the time. Each major user must have NIH research support at the time of award and at least one-half, but a minimum of two, of the major users must hold NIGMS grants.

The DRR Shared Instrumentation Grant Program is a subprogram of the Biomedical Research Support Grant Program, so eligibility is limited to institutions which receive a BRS grant award. A major user group of three or more investigators is required, and each major user must have PHS peer-reviewed research support at the time of the award. The applicant must show a clear need for the instrumentation by projects supported by multiple NIH research awards and demonstrate that these projects will require at least 75% of the total usage of the instrument. An internal advisory committee is recommended to help assure shared use and maximum utilization.

If the major user groups do not require total usage of the instruments, access can be made available to other users. These users need not be NIH awardees but priority is given to NIH-supported scientists engaged in biomedical research, including new young investigators.

7. Intended User: The results of this project will be used by the staff of DRR and NIGMS in planning their respective future instrumentation support activities and reviewing current practices regarding shared instrumentation grants. In addition, by completing the picture already partially drawn by reports from other studies (e.g., NIH 83-311, Academic Research Equipment and Equipment Needs in the Biomedical Sciences; NIGMS 82-401, Evaluation of NIGMS Shared Instrumentation Initiative), the study will support policy formulation by the corporate management of NIH regarding the support of instrumentation for biomedical research. The final report should be available early in calendar 1987.

8. Information to be Generated: Set out below is a preliminary list of the issues/questions to be addressed in the evaluation. NIH staff will continue to develop this list in preparation for the execution of the contract. Changes will then be made as the contractor works with NIH

staff and technical advisors to identify the items having highest priority that are appropriate to a questionnaire survey approach.

Comparisons for all of the following items will be made between earlier and more current cohorts of grantees; between instruments that vary widely in costs; between instruments that were purchased with DRR, NIGMS, and other funds; etc. The contractor will also investigate whether putative comparison groups can be constructed from data developed in other studies (e.g., NIH 83-311).

Impact

- To what extent have the instruments met the scientific needs and enhanced the research endeavors of the major users?
- How have they benefited the overall research communities they serve?
- What has been their contribution(s) to users' research?
- Have they benefited research training?

Sharing

- How has access to the instruments been managed in order to ensure their use by the widest possible community of NIH/PHS-sponsored users?
- Who has used the instruments and for what proportion of time, assays, spectra, etc.? What are the characteristics of the user pool? (Department; Institution; Research area; Ph.D., M.D., new investigator; NIH (PHS) B/I/D support; "Quality" of research; Pilot projects, etc.)
- Have there been changes in Use/Sharing over time?
- Have there been changes in characteristics of user pool over time?

Advisory Committee

- How were committees structured and how did they function?
- Were there changes in structure/function over time? (Since the time of the application.)

Capitalization/Implementation

- What were the amounts and sources of other capital funds?

- How long did it take from award to purchase, purchase to installation; and installation to "on-line" operation?

Operation

- How have institutions met commitments for operation and maintenance of the instruments on a long-term basis?
- How have the instruments been managed on a day-to-day basis, including the availability of qualified individuals to supervise their operation and provide technical advice to the users?
- What has been the magnitude and variations of operating and maintenance costs, and where did the institutions obtain the funds to pay for them?

Utilization

- Are the instruments being used to capacity?
  - How much down-time?
  - How much idle time?
- Were they used by the investigators, and/or for the science, described in the applications? What changed from application to implementation, and why?

Program Policies

- Are current policies discouraging some eligible institutions from applying for awards?
- Are there problems with/resulting from current policies and procedures?
- Are there suggestions for changes?

Obsolescence

- Are these instruments (still) the state-of-the-art?
- Have they been supplanted by more modern tools? When? How funded?
- Have changes in users/uses over time resulted from development of newer instruments, from changed needs due to scientific progress?

9. Approach: The phases/products described below reflect NIH staff's proposed strategy. It is expected that changes will be made as a

result of advice from the contractor, and proposers will be free to put forward their recommended methodologies as part of their proposal.

Phase 1 - Overview and Definition (1 to 3 Months)

As part of the first phase of the evaluation, the contractor will work with NIH staff to identify additional issues or questions that might be addressed by the study; to assign relative priority to issues and questions; to develop appropriate performance indicators and measures; to recast questions in a form appropriate for the study methodology; and to determine the proper respondent(s) at the grantee institution for each question.

In light of the questions to be answered, the contractor will determine what relevant information is available (either for providing answers to the questions or for illuminating the scope and context of the evaluation) from grant files, NIH data bases and other studies.

The Phase 1 report will include draft descriptions of the NIH shared instrumentation programs, including their objectives and operation; of their place in the broad context of the need for, and support of, instrumentation for biomedical research; of what is known about the programs and what remains to be determined; and what information is likely to be obtainable by this evaluation. The report will also contain the contractor's general proposal for the nature and timing of the remaining tasks and deliverables.

Phase 2 - Study Plan and Data Collection Strategy Development (1 to 2 Months)

In Phase 2, the contractor will prepare a detailed plan for the completion of the evaluation. The plan will include consideration of what technical (biomedical instrumentation-related) advice and assistance will be needed, and when, where, and how it will be obtained and integrated into the study. A detailed data collection strategy including the survey and other sources will be included.

Phase 3 - Questionnaire Development (2 to 3 Months)

Here, the contractor working closely with NIH staff, will develop and perfect the questionnaires and determine the samples to be surveyed. Visits to 2-4 near-by grantees will be made during the development of the survey forms, and there will be visits to 3-6 institutions as part of the pilot testing. The questionnaires will then be submitted for OMB clearance.

Phase 4 - Short-Term Evaluation (2 to 3 Months)

While awaiting clearance of the questionnaires, the contractor will obtain, and analyze to the extent possible at this stage, relevant data from all other sources. Draft material from earlier phases will be put in final form in anticipation of its inclusion in the final report, and formats for the analysis and display of survey results will be prepared. In consultation with the Project Officer, the contractor will prepare letters requesting institutional cooperation and instructions to survey respondents.

Phase 5 - Survey Execution (2 to 4 Months)

Contractor mails questionnaires and engages in follow-up activities.

Phase 6 - Final Report Preparation (2 to 3 Months)

Survey results will be analyzed and integrated with data from earlier phases. The Final Report will be prepared, to include recommendations regarding data that could not be obtained within the constraints of this evaluation.

10. Information Clearance/Collection: Yes

11. Pre-Rule Making Activity: No

TABLE 1

DIVISION OF RESEARCH RESOURCES

BRS-Shared Instrumentation Grant Program

Summary of NIH Research Grants Supporting Major Users

Year	Number of Awards	Total # of Major Users	Number of Users' Grants by NIH Institute											
			CA	AI	DE	ES	AM	GM	HL	HD	AG	NS	EY	Total
FY 1982	23	212	74	30	6	3	40	47	30	24	3	24	6	287
FY 1983	91	782	205	86	43	25	126	227	118	54	15	80	41	1020
FY 1984	115	887	269	118	38	24	147	314	131	65	21	89	58	1274
FY 1985	171	Not yet available												

TABLE 2

DRR and NIGMS Shared Instrumentation Grant Programs

Summary of Funding

Year	Total Dollars Funded	
	DRR	NIGMS
FY 1979	-	$6,899,101
FY 1980	-	1,619,745
FY 1981	-	700
FY 1982	$ 3,700,000	882,799
FY 1983	14,000,000	616,494
FY 1984	19,700,000	200,000
FY 1985	31,800,000	270,000
Total	$69,200,000	$10,488,839

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier: NIH/NIDR 86-309

2. Project Title and Capsule Description:

   a. Title: Assessment of NIH, Industry, and Academic Relationships in Restorative Materials Research

   b. Capsule Description: The relationship between government, industry, and academic endeavors in restorative dental materials research will be assessed by analyzing survey data, publications, and patent records. The purpose is to estimate the magnitude, nature, characteristics, and outcomes of these collaborative relationships.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)
86	$250	

Justification: This project can serve as an initial case study of relationships between government, industry, and academia in the funding and conduct of biomedical research in a particular program. The National Eye Institute (NEI) has reviewed the project description for this project and expressed the opinion that the end product as well as the methods proposed for the study should have general applicability to other institutes at NIH and should prove to be specifically useful to the NEI in a number of ways.

The project will be conducted through a contract because the necessary expertise and staff are not available in-house. The cost estimate was based on best estimates of the resources that will be required to perform the three aspects of the study--a survey of firms and investigators engaged in restorative dental materials research, a bibliometric analysis of the related literature, and an analysis of the patents generated by source of funding.

Preliminary estimates indicate that around 180 commercial firms currently manufacture and supply various restorative dental materials. These firms will be surveyed to determine the amount and type of research they conduct in-house or support extramurally. A universe of all restorative dental materials faculty at dental schools, all members of the restorative materials section of the American Association for Dental Research, and all previous and current restorative materials grantees with the NIDR as well as additional investigators identified during the firm survey will be interviewed by telephone. Preliminary estimates of the number of separate individuals from these sources is around 350 people. It is estimated that approximately one person-year of effort plus support and indirect costs from individuals experienced in questionnaire construction and interviewing will be required. This amount and quality of effort translates into a cost estimate of $75,000 to conduct the survey.

Past experience indicates that a full bibliometric analysis including citation analysis will require approximately one and one-third person-years (plus support and indirect costs) from individuals experienced in all aspects of bibliometric analysis and who have assess to the appropriate bibliometric databases. This amount and quality of effort translates into a cost estimate of approximately $100,000 to do that portion of the project. The patent analysis will require a thorough investigation of both NIH's patent file as well as more general patent files. Approximately one person-year (plus support and indirect costs) will be required from individuals experienced in this type of analysis. This amount and quality of effort translates into a cost estimate of $75,000 to conduct this portion of the project.

4. Project Monitor/Contact:

Dr. L. Jackson Brown
Evaluation Officer
Office of Planning, Evaluation, and Communications
National Institute of Dental Research
Building 31, Room 2C-36
Bethesda, Maryland 20205
(301) 496-6705

5. Coordination:

Dr. Harald Löe, Director
Dr. Marie U. Nylen, Associate Director for Extramural Programs
Dr. Lois K. Cohen, Assistant Director, International Health and Chief, Office of Planning, Evaluation, and Communications
Dr. Joyce A. Reese, Health Science Administrator for Restorative Dental Materials Research
Dr. Dushanka V. Kleinman, Chief, Planning and Evaluation

6. Program Evaluated:

NIDR Restorative Dental Materials Research
PHS-NIH-Biomedical Research-Institute Specific-Dental

7. Intended Users:

a. Primary Users:

Executive Staff, NIDR
HSA's in the Extramural Program, NIDR
Executive Staff, NIH and other Bid's

b. Timetable:

1. RFP Developed	November 1985
2. Evaluation Begun	August 1986
3. Final Report	March 1988

8. Information to be Generated:

Very little is currently known about the role of the commercial biomedical industry in funding biomedical research in general. Still less is known about the role of industry as it relates to particular programs. In this regard, several types of information (both substantive and methodological) are of interest to the NIH and the NIDR. Among the substantive questions of interest are the following: What areas of research are commercial firms supporting? What proportion of funding in these areas does industrial support represent? How much collaboration is occurring between industry, academia, and government? Is research supported by industry shorter term and/or more applied than research supported by government? How much of the scientific literature in an area can be traced to research supported by industry? How significant is this literature as measured by citation analysis? How important is industry-supported research in generating patents?

Attempts to develop the substantive information are confronted by several methodological obstacles. Foremost is that assessing the industrial role across the broad spectrum of biomedical research would be an enormous undertaking. A practical alternative is to assess the inter-relationships between government, industry, and academia by investigating discrete areas of research, building information a piece at a time. A study that the Office of the Assistant Secretary for Planning and Evaluation, DHHS is currently funding is an example of this more limited approach to the overall question. In that study, the role of industry in supporting research in a few areas of biotechnology with potentially important commercial applications is being investigated through a series of surveys. However, research with biotechnical implications is supported in various degrees through programs in several Institutes. The applicability of this approach for a specific program evaluation is not yet known.

The proposed study will assess the utility of surveys of firms and academia to evaluate role of industry in supporting restorative dental materials research. In addition, bibliometric analysis and patents will be used to develop outcome measures of the extent of collaboration between government, academia, and industry in this program to check whether the results of the surveys are replicated in publication activity. These results will be compared to the goals and objectives for the restorative dental materials program contained in the "Long-Range Research Plan FY 1985-1989" for the NIDR. Consequently, the study will serve two purposes. It will evaluate the relative roles of industry, academia, and government in fulfilling the goals and objectives of the restorative dental materials program. It will also allow assessment of the separate and combined contributions of survey data, bibliometric techniques, and patent records towards the evaluation of industry/academic/government inter-relationships in other NIH programs.

Several features of the restorative materials research program make it an attractive area with which to test these methods. It is a discrete area of research of manageable size; industry is known to be active in this type of research; the area is old enough to expect industry-supported research to have generated a number of patents; the literature in the area is well-covered by existing bibliometric databases; the commercial firms and the investigators active in this area are known and small enough to allow a census to be taken. For these reasons, this project is a practical first step and can serve as a case study for the broad assessment of role of industry in biomedical research.

9. Approach:

The project will acquire primary data from commercial firms, individual investigators, and Federal government organizations that are active in restorative dental materials research. Secondary data on patents, publications, and their citations will also be analyzed to compare research supported by industry with that supported by government and to assess the extent of collaboration among the different sources of research.

The commercial firms that are active in this research are known. These firms will be the target universe of the first mail survey. A census will be taken since relatively few firms are involved. The most appropriate respondent in the firm, probably the director of research, will be mailed a questionnaire. The following is a sample of the general types of information that will be acquired from the respondents; the extent of their firm's activity in restorative dental materials research, both in-house and through support of research conducted outside the firm, the characteristics of the research being supported such as length of support, amount of support in dollars and resources, the specific research topics that are supported, the extent of collaboration between their firm and NIDR/academia, the investigators that have been supported and where they are located and the patents that have resulted from the research.

Like commercial firms, the investigators that are active in dental restorative materials research are known. They will be the target universe of a second census survey. The same general types of information will be acquired through a mailed questionnaire to these respondents. However, instead of dealing in aggregate amount of research funded by firms, this questionnaire will be investigator-specific. Furthermore, additional information will be acquired with this survey that will not be available from firms. For example, the investigators will be asked details of their support from industry as well as from the government and private foundations. This will allow the extent and characteristics of research supported by industry to be compared with research supported by other sources including the NIH.

The detailed questions for these general types of information will be developed during the project. Each question will be thoroughly analyzed to determine that it is understandable and elicits the intended information with the required specificity. Both questionnaires will be pre-tested. The contractor will conduct the surveys by mail. Endorsements from the NIDR and other influential dental organizations as well as extensive follow-up will be used to increase response rates. The contractor will conduct the field operations, edit the data, and analyze it with statistical techniques appropriate to address the above research questions.

Similar information will be collected from the small number (less than nine) of government organizations that conduct restorative dental materials research in-house to complete the description of research activities.

The contractor will use secondary data from various bibliometric databases to compare the publications resulting from research supported by industry with publications resulting from research supported by other sources including the NIH. The analysis will assess the publication rates and the citation rates of research supported from different sources. In addition, the scientific journals that are most important for the publication of research from each funding source will be described. Finally, the contractor will use secondary data to assess the quantity and the characteristics of patents originating from both sources of support.

10. Information Clearance/Collection: Yes

11. Prerulemaking Activity: None

Reviewed and approved by
NIH Committee

1. NIH Evaluation Project Identifier: NIH/NCI 86-312

2. Project Title and Capsule Description:

   a. Title: Request for Add-on Funds for the Hospital Cost & Clinical Research Project

   b. Capsule Description: The Hospital Cost and Clinical Research Project (HCCRP) is a collaborative study being conducted by NIH and the National Center for Health Services Research (NCHSR). It is being supported by 1% set-aside funds from the Office of the Assistant Secretary for Health. The study is designed to examine the effects of Medicare's prospective payment system (PPS) on cancer clinical research by examining the costs of providing hospital care for patients on clinical trials and studying changes in patterns of treatment for cancer patients pre and post PPS. No systematically obtained data are available to show that the costs of services required and provided to patients according to a research protocol differ from those provided to patients with the same diagnosis in the absence of a protocol. Though the HCCRP research scope is limited to patients with the diagnosis of cancer so that protocol and nonprotocol comparisons can be made, study results will provide information to other institute therapeutic clinical trials research.

3. Cost and Funding Source:

   a. HCCRP has been approved for funding from 1% set-aside funds (OASH) as indicated below. An additional amount is being requested from NIH evaluation set-aside funds.

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)
1984	125,000	---
1985	391,169	---
Total	516,169	---
b. Add-on Request		
1985 ~~1986~~	190,469	---

The add-on is requested in order to attach names to hospital discharge abstracts for approximately 30 hospitals. Assumptions that patient identification and financial information were linked with all of the abstracts were wrong. The original budget estimates were based on the consistent availability of these linkages. Names are needed in order to match the abstracts against NCI lists of protocol patients and to establish linkages between hospital discharge abstracts and billing data. In about 22 hospitals, hospital staff or outside technicians must be trained and paid for the costs associated with hand-matching protocol patient names against discharge abstracts. There are approximately 8 hospitals that do not include names on the abstracts and are affiliated with cancer centers that will not release protocol patient names. For each of these hospitals, all cancer patient discharge abstracts will be required to have names attached manually. Finally, there are about 20 hospitals that require names to be attached to the abstracts in order to form the link between billing data and discharge abstracts. This involves processing two years of discharge abstracts (1982 and 1985).

Included in this add-on task are (1) development and coordination of consistent procedures, (2) on-site visits in cases where the contractor's staff is performing the actual matching, and (3) matching that is performed by hospital-based medical records clerks. Approximately 794 full-time days for medical records clerks and a total of 163 days for project management, coordination, computer programming, and support are estimated. About 95,400 records will be hand-processed. Work will be done through the current contractor supporting the project (SysteMetrics, Inc.).

4. Project Monitor/Contact:

Allen Feldman, M.D.
Medical Staff Fellow
Community Oncology and
Rehabilitation Branch
Centers and Community Oncology

Division of Cancer Prevention
and Control
National Cancer Institute
Blair Bldg., Rm. 7A01
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Jerome W. Yates, M.D.
Associate Director
Centers and Community Oncology

Rosemary Yancik, Ph.D.
Assistant Director
Centers and Community Oncology

Division of Cancer Prevention
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National Cancer Institute
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(301) 427-8636

5. Coordination: Planning for the original project was developed in consultation with representatives of ASPE (Randy Teach); OASH (Glenna Crooks); NCI Staff (Jerome W. Yates, M.D., DCPC; Robert Wittes, M.D., DCT; and others); and NCHSR staff (Drs. John Marshall, Donald Goldstone, Rosanna Coffey and others).

Throughout the past year, other key individuals associated with launching this project include Michael Friedman, M.D., DCT, NCI; Lucius Sinks, M.D., Cancer Centers Branch, DCPC, NCI; Robert Frelick, M.D., Community Oncology and Rehabilitation Branch, DCPC, NCI; and Charles Coltman, M.D., Chairman, Cooperative Groups Committee.

The HCCRP has been presented for information purposes to NCI's DCPC Board of Scientific Counselors Subcommittee for Centers and Community Oncology. It has been described to the chairmen of the cooperative groups being supported by the NCI's DCT. Through the offices of Dr. Yates and Dr. Wittes, coordination has been established with the cooperative groups and cancer centers. Overall project coordination is the responsibility of Dr. Yates and Dr. Coffey.

6. Program Evaluated: NIH Clinical Trials

Clinical trials are scientific research activities undertaken prospectively to ascertain the effects and value of preventive, diagnostic, and therapeutic agents, devices, regimens and procedures.[1] They test hypotheses in controlled settings validating the efficacy of treatment or prevention regimens. In NIH-supported activities, clinical trials may refer to one or more investigators at one or more locations following the same protocol. Numbers of cases or patients accrued to test the hypothesis vary by investigator or institution. Data from multicenter trials are aggregated for analysis.

The clinical trial is an important effort in biomedical research. Large-scale clinical trials require adequate numbers of patients and extensive resources to answer the questions. They must be cost-effective. Large proportions of institute budgets support this research. Both NCI and NHLBI have been funding large efforts in clinical trials research. For example, about 14% ($151.7 million) of the NCI's FY 1984 budget was devoted to its clinical trials research program. This includes intramural and extramural research. The NHLBI program budget for FY 1984 was 4% ($22.8 million), but this represented an all time low. In FY 1974, 16.5% of the budget was devoted to clinical trials. NHLBI projections for FYs 1985, 1986, and 1987 indicate increased allocations will be made. Other institutes (with the exception of NIEHS and possibly NIGMS), while less active in clinical trials, also use the mechanism. In addition, the General Clinical Research Centers (GCRC) of the Division of Research Resources of NIH support clinical trials. GCRC programs provided resources to facilitate conducting clinical trials in other institutes and other agencies by allocating 21.7% ($17.7 million) to support clinical trials research.

7. Intended Users: The NIH will be the primary user of this evaluation. The basic methodology and findings are generally applicable to therapeutic clinical trials research. NCI-sponsored protocols utilize any of multiple disciplines (surgery, medicine (chemotherapy), radiation therapy, and biological response modifiers). Findings from this project will guide the NCI in future program planning. Researchers who conduct clinical trials will be able to use these study results to assess the overall effect on hospitals of participation in protocols. If costs for patients on protocols are no more than the costs for routine care, on average, then hospitals may be persuaded to

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[1] Paraphrased from the NIH Inventory of Clinical Trials, Section One. Introduction, p. 1.

continue their participation in these programs. If however, protocol-associated care costs are considerably more for this group of patients, some provision for supplementing payments will be required. Information from this project will also guide DHHS, particularly PHS, HCFA, and ASPE, in assessing consequences of a fixed payment system on clinical research activities and whether special considerations for such activities are in fact warranted by their contribution to improved outcomes for cancer patients.

8. Information to be Generated: Tasks for this particular add-on request were described in a preceding section. The HCCRP is measuring hospital cost differences between patients participating in clinical research and similar nonparticipating patients. Patient characteristics such as diagnoses, stage of cancer, and age will be controlled statistically in order to measure cost differences attributable to research. In addition, hospital teaching status, bed size, location, and other factors will be held constant in comparing costs of patients across different institutions.

Once the costs of treating specific cases are identified, these costs will be compared with the DRG payment that would be received for each patient in a particular hospital in 1986 under the full DRG-based system for hospitals. These DRG payments will be calculated from the HCFA formula for the Medicare prospective payment system. This formula is based on the patient DRG category plus adjustments for area wage differences, teaching costs, and location. Types of hospitals which gain or lose revenue in the treatment of their cancer patients under a fixed payment system will be examined with respect to their characteristics. The percentage gain or loss in patient revenues will also be estimated. In this way, the incentive facing the hospital to continue or terminate participation in clinical trials research can be evaluated.

It is important to obtain information on the impact of PPS on clinical research which may be vulnerable to using pre-determined, per-case payments to hospitals. Heavy investments are made by the institutes in clinical trials research. The question of whether or not PPS influences or adversely affects participation in clinical research must be answered.

9. Approach: A complete HCCRP description is provided (Attachment I). In brief, HCCRP is based on a sample of approximately 53 of the 310 hospitals participating in NCI-sponsored clinical trials in 1980-1985. The hospitals are stratified by location and type of NCI affiliation (cancer center, cooperative group, or CCOP hospital). The contractor, SysteMetrics, Inc., is obtaining the hospital discharge abstracts for years 1980 through 1985 and patient-level billing data for 1982 and 1985 for all patients with the diagnosis of cancer in the participating hospitals. These abstracts and bills are being matched against lists of patients enrolled on clinical research protocols during the same years (supplied by NCI research institutions) in order to enable the researchers to distinguish protocol from nonprotocol patients. No primary data collection will be required for this study.

The hospitals being asked to participate in the study are distributed across all four geographic regions of the U.S. (16 North Central; 16 North East; 12 South; and 9 West). A total of about 5000 protocol patients are projected to accrue yearly from these hospitals for the period 1980 through 1985.

Given cost and protocol designation, cost comparisons will be made between groups of protocol and nonprotocol patients holding constant the type of cancer, stage of the disease, age of the patient and hospital characteristics. From equations that estimate the marginal cost of protocol patients, patient revenues and costs under cost reimbursement can be calculated and compared to DRG-based fixed rates for protocol and nonprotocol patients. The financial implications of cost-based versus prospective-based payment for clinical research will be examined by type of hospital.

10. Information Clearance/Collection: No

Reviewed and approved by
NIH Committee

1. NIH Evaluation Project Identifier: NIH 75-1

2. Project Title and Capsule Description:

   a. Title: NAS Continuing Study of National Needs for Biomedical and Behavioral Research Personnel

   b. Capsule Description: Congressionally mandated study of biomedical and behavioral research manpower needs, and assessment of training programs, conducted buy the National Academy of Sciences

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)		DCRT Charges (in thousands)	Other Expenditures (in thousands)	
Prior Years	6,951	(64)	2	6,949	(64)
86	497	(75)	2	495	(75)
87	495	(80)	0	495	(80)

Notes: ( ) denotes OD General Expense fund
* includes 20 added by ADAMHA for data development, 17 by NCHSR and 19 by NIGMS for special attention

The proposed annual expenditures are commensurate with the level of effort provided by the NAS in recent years.

4. Project Monitor/Contact:

Charles R. Sherman, Ph.D.
Program Evaluation Branch, OPPE
NIH, Building 1, Room 228
9000 Rockville Pike
Bethesda, MD 20205

5. Coordination: The Manpower Evaluation Advisory Committee, chaired by Dr. Charles R. Sherman, will provide periodic review of technical aspects of this project.

6. Program Evaluated: PHS-NIH-Biomedical Research Activity-Training
PHS-HRS Health Resources-Health Manpower
(Limited to Division of Nursing, Research Personnel)
X-Many HHS Programs-Manpower and Training
X-Non-HHS Programs-Employment and Training

7. Intended Users: The intended users of this study are Congressional committees, the Secretary of HHS, the Director of NIH and the NIH Associate Director for Extramural Research and Training. The NAS conducts a continuing study and issues a principal report every two years in accordance with current legislation. It also issues occasional reports on special subjects studied in depth for use in the principal study. The next principal report is scheduled to be available in October, 1985.

8. Information to be Generated: This study answers two basic questions raised by the Congress and paraphrased as follows: How many people does the nation need for biomedical and behavioral research? How well are our training programs meeting the assessed need? The NAS is also asked to recommend any changes that may be required to assure an adequate supply of trained personnel and an appropriate balance in the kinds of training opportunities available. The principal reports bring together a variety of numerical data on graduate enrollments, degrees awarded, labor force supply and demand indicators and updated projections of training needs. There are also discussions of ancillary current issues such as changing career patterns, effects of demographic change on research productivity, the role of non-M.D. scientists in clinical investigations, minorities entering scientific careers, and research career retention rates of alternative training modalties. This information is used to describe and guide the training programs of the NIH and ADAMHA.

9. Approach: A committee of the NAS with panels of bioscience and manpower experts work closely with NAS/NRC staff and representatives of the NIH Director in planning studies and analyses needed for deliberations of the committee. A projection model of supply and demand is routinely revised for each semi-annual report. A special study to be completed in the coming year is a follow-up of NIH-supported post doctoral trainees to disclose their records of employment, research grant competition and research publication. Suggestion for other special studies that NIH and ADAMHA may choose to undertake may also be offered as a result of committee deliberations. The project will also update two major manpower research files: the Trainee and Fellow File and the Consolidated Grant Applicant File. The data bases are used primarily by the NAS committee but are made available for use in other evaluation studies.

10. Information Clearance/Collection: No

11. Prerulemaking Activity: No

UNDER REVIEW

1. NIH Evaluation Project Identifier: NIH/DRR 85-310

2. Project Title and Capsule Description: Evaluation of the Uses of Animals in Research. This evaluation will examine how animals are used today in biomedical research and how they will be used in future research efforts.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Expenditures (in thousands)	Other Expenditures (in thousands)
85	$135,000	---	---
86	$200,000	---	---
87	$294,777		

Based on the experience with the pilot study, the conduct of a full-scale national survey will require $200,000 in Fiscal Year 1986 and $294,777 in Fiscal Year 1987, provided OMB approval of the survey is obtained.

NIH does not have available sufficient staff time to accomplish this study in-house.

4. Project Monitor/Contact:

Dr. James D. Willett
Chief, Biological Models and
Materials Resources Section
Animal Resources Program
Division of Research Resources
Building 31, Room 5B23
9000 Rockville Pike
Bethesda, Maryland 20892
301-496-5175

5. Coordination: This project has been reviewed by the NIH Director, the NIH Evaluation Policy and Oversight Committee, the NIH Technical Review Committee, and an ad hoc advisory committee. This ad hoc committee is comprised of: Dr. William Raub, Deputy Director for Extramural Research and Training (Chairman); Mr. Kurt Habel, Acting Associate Director for Program Planning and Evaluation; Dr. Joseph Held, Director, Division of Research Services; Dr. Charles McCarthy, Director, Office for Protection from Research Risks; Dr. Betty Pickett, Director, Division of Research Resources; and Mr. Storm Whaley, Associate Director for Communications. This ad hoc advisory committee will provide continuing oversight of this study.

6. Program Evaluated: PHS-NIH-Biomedical Research

This study addresses the full range of NIH intramural and extramural programs using animals for biomedical research. Projects using animals represent 44% of NIH's entire extramural efforts. Knowledge of how research animal use has changed and is changing throughout the nation's research enterprise will aid NIH in determining the current and future needs of the biomedical research community for laboratory animals.

7. Intended User: The results of this study will be used by the Director of NIH in planning research programs and reviewing current policies regarding the use of animals in NIH-supported research. The Assistant Secretary for Health has also expressed to the Director of NIH an interest in the results of this study. This study will also respond to Congressional interests as expressed in S-540 in the 98th Congress, which specifically called for a study of animals in research.

8. Information to be Generated: This project will result in the acquisition and analysis of objective data on the use of laboratory animals and on laboratory animal resource within the United States. Data will be acquired through a national survey of facilities, both public and private, using laboratory animals. The study is occurring in two phases. The first involves the design and test of a survey instrument at nine research centers. If the survey's design proves successful and Office of Management and Budget (OMB) approval is obtained, a full-scale national survey will follow.

   The Commission on Life Sciences (CLS) is the lead organizational unit within the Academy for this study, with the National Research Council's (NRC) Institute of Laboratory Animal Resources (ILAR) having responsibility for the study's design and implementation.

   The survey will provide information on the numbers and species of animals used; colony charccteristics; sources of animals used; purposes for which the animals were used; duration of their use (acute or long-term studies); sources of funding for the studies using animals; trends in the use of each species during the last five years; current inventories by species; status of laboratory animal facilities and resources; and needs perceived to meet research requirements and to achieve optimal compliance with laws, regulations, guidelines and policies on the use of animals.

9. Approach: A definitive, comprehensive evaluation by the scientific community of the use of animals in the nation's research enterprise is needed. A compilation of numbers of animals used by species, projections of needs for laboratory animals, and analysis of trends in research animal use in research, and the costs and focus of such use of animals will be provided through this study. Costs imposed on the research enterprise as a result of current and proposed laws and policies governing research using animals will be determined. Two questionnaires have been developed to provide this information, and a direct sampling of a select number of research centers through site visits and record audits is being considered as a means of verifying data gathered through the questionnaires.

   The National Institutes of Health, along with other federal and private agencies, is providing program and information resources to the ILAR committee responsible for design and test of the survey instrument.

   Funding for the study is through the Public Health Service/National Academy of Sciences cooperative agreement for core support of selected boards of the National Academy of Sciences (ASU000001-04). Costs for developing and testing the survey are $135,000. NIH has cooperated with NAS's ILAR committee in the survey's design, where such cooperation was appropriate under NRC policies and guidelines.

The ILAR committee conducting the survey's design (see Attachment for the committee's roster) has met twice as a full committee and has held two subcommittee meetings.

While the last ILAR survey questionnaire served as a point of departure, the Committee employed experts in survey design to alter and modify the original questionnaire to meet the current study's objectives. Input from a variety of sources on the survey's design and implementation was sought and obtained by the Academy. It was decided to conduct this survey in two stages. A short questionnaire was drawn up to determine, within the range of organizations sampled, where animal use is occurring, and which individuals within the organization are most capable of answering questions about animal use. This questionnaire was sent to the top level administrator with responsibility for all research within the organizations sampled. A full questionnaire, seeking information on the kinds and numbers of animals in use within the organizations, as well as information about the nature of the laboratory animal facilities therein, is nearing completion and will go to those individuals identified in the course of the first mailing. It is expected that the pilot survey responses will be in and analyzed by mid-December 1985, and site visits to the organizations surveyed are to take place in December and January. The site visits will assess the effectiveness of the survey in obtaining the data sought. A fully tested and refined survey instrument will be delivered to NIH in March 1986. A request for an extension of time of 60 days for the pilot study is being made by the study committee. This request stems from the use of two questionnaires, which requires additional time in which to receive responses and to follow-up on any non-responders.

On completion of the national survey, the ILAR Study Committee will prepare a report analyzing the data gathered. This report will serve as a basis for an assessment by the scientific community of the current use of laboratory animals throughout the nation's research enterprise, and will serve as a key component in the Academy's study of the issues (Phase II) associated with the uses of animals in biomedical and behavioral research. The report from the national survey will provide critical objective data on the nation's use of research animals to NIH, the public, the scientific community, Congress, regulatory authorities, other governmental and private agencies, and policymakers in private enterprise.

10. Information Clearance/Collection: Yes, if a survey is conducted.

11. Pre-Rulemaking Activities: No.

FY 85 Project Approved
for Rebasing Activity only
but not previously
included in Plan

1. NIH Evaluation Project Identifier: NIH 85-313

2. Project Title and Capsule Description:

   a. Title: Assessment of the effect of modified stratification on the Biomedical Research and Development Price Index.

   b. Capsule Description: This study will introduce into the Biomedical Research and Development Price Index supplementary strata composed of equipment and supplies specialized to biomedical research to assess their effect upon the price index and to determine whether their permanent incorporation into the index will justify the additional annual cost.

3. Agency Proposing: NIH

4. Cost and Funding Source:

Fiscal year	Expenditures (in thousands)	DCRT charges (in thousands)
85	$100 1/	$2
86	$250 2/	$2
87	$150 3/	$2

1/ $90 for rebasing, $10 for supplementation planning.
2/ $100 for rebasing, $150 for direct pricing.
3/ $150 for direct pricing.

5. Program Evaluated: Biomedical Research and Development Price Index (BRDPI)

6. Purpose: The degree to which the Biomedical Research and Development Price Index accurately measures price movements affecting NIH resources is critically important to its use as a deflator of NIH budget and cost data. The proposed new strata clearly constitute a technical improvement in the index methodology; the study is intended to determine the practical effect and to provide the necessary data for an informed judgement as to whether the additional costs that would be built into subsequent annual updates are justifiable.

7. Intended Users: NIH, DHHS, OMB, Committees of the Congress, and the biomedical research community.

8. Type and Approach Methodology:

   a. Type: Assessment of a program information system.

   b. Approach/Methodology:

The BRDPI is a fixed weight price index of the Laspeyres type, currently based in FY 1979. It is designed to measure average price movements of goods and services NIH buys directly and through projects it supports. It is stratified by type of research performer (NIH, universities, industry, and other), and by personnel and nonpersonnel cost categories. Wages and salaries and fringe benefits are substrata of personnel costs. Object-classes and groups of related object-classes form nonpersonnel sub-strata for NIH, taking advantage of the wealth of detail available from the Common Accounting System. Nonpersonnel sub-strata for NIH grantees are the cost categories of awards from the NIH IMPAC system. Price data used in the index are obtained by direct pricing for NIH and university personnel inputs (accounting for about half of the total weight), and through the use of indexes for all other substrata.

The Working Group on Price Index Assessment, formed by ADPPE/NIH on May 8, 1984, and reporting October 15, 1984 (Tab A) concluded that equipment and supplies specialized to biomedical research are a sufficiently unique and volatile product mix to cast doubt on the applicability of surrogate indexes to their average price movement. The Working Group recommended, therefore, that direct pricing of selected items of equipment and supplies specialized to biomedical research be undertaken and the data be incorporated in the BRDPI. The Working Group also recommended that the BRDPI be rebased and reweighted to FY1984. Dr. Wyngaarden has concurred in the recommendations of the Working Group (Tab B).

The proposed study involves two related major activities: (1) rebasing the BRDPI to FY1984; (2) developing price series whose weighted average price movement will form the BRDPI.

It is essential to replace the present FY1979 weights with similarly constructed weights for FY1984 to reflect more accurately the mix of goods and services used in biomedical research and development performed or supported by the NIH. The weights would be developed from the finest level of detail allowable by the available data and summed into appropriate strata. The equipment and supplies strata would be subdivided into two parts, one composed of items highly specialized to biomedical research to be selected by scientists on the technical advisory committee (see 11 below) and one composed of the residual items of equipment and supplies purchased by research performers. The equipment and supplies strata account for more than half of the total FY1979 weight.

The development by BEA of direct price series for the new strata of items specialized to biomedical research is a complicated and difficult set of tasks. Surrogate price indexes would continue to be used for the residual equipment and supplies component.

It is important to keep in mind that the cost of direct pricing cannot be finally determined until the technical advisory committee fixes upon the number of items of specialized equipment and supplies that are to be included in the BRDPI. For purposes of cost estimating we have assumed that 20 to 25 items would be priced and suitable weights developed, which we believe implies an annual cost of $150,000 a year for FY1986 and FY1987.

The price index would be calculated both ways (i.e., with and without using the supplementary strata) and the difference assessed by the Technical Advisory Committee. Any increase in the proportion of the index weight that is subject to direct pricing would improve the theoretical accuracy of the index, and direct pricing of volatile biomedical research equipment and supplies is an appropriate choice as an area for improvement. The issue of this proposal is whether the undoubted theoretical improvement can be assessed as worth its cost to NIH. A note at Tab C details the steps to be followed by the proposed project.

9. Execution: The project will be accomplished through an Interagency Memorandum of Agreement with the Bureau of Economic Analysis of the U.S. Department of Commerce. The final benefit-cost assessment of the resulting differences in the two indexes and recommendations regarding whether or not to incorporate the changes will be made by the NIH Technical Advisory Committee. The project will be administered by the Office of Program Planning and Evaluation of NIH.

10. Project Officer/Contact:

William L. Copeland,
Special Assistant to the Director
Division of Program Analysis, OPPE
National Institutes of Health
Building 31, Room 4C35
9000 Rockville Pike
Bethesda, Maryland 20205
Telephone: (301)496-5011

11. Coordination: The project has been reviewed by the Working Group on Price Index Assessment, the Associate Director for Program Planning and Evaluation, the Evaluation Oversight Committee, and the Director, NIH. Discussions have been held with NSF to confirm that no R&D price index efforts are being pursued there that would be relevant.

A Technical Advisory Committee will oversee the project. It will be composed of several NIH scientists who will be responsible for selecting items of equipment and supplies specialized to biomedical research, and several other NIH staff familiar with NIH record systems and with statistical analysis.

FY 85 Project Approved
but not previously
included in Plan

1. NIH Evaluation Project Identifier: NIH 85 - 316

2. Project Title and Capsule Description:

   a. Title: An Examination of Research Opportunities in Biology

This study will evaluate the state of the Biological sciences and develop policy recommendations for maximizing advances in areas with the most promising opportunities.

3. Cost and Funding Source

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	$167.4	--	$167.4

These expenditures match funds already committed to this project by the National Science Foundation ($400,000) and the Department of Agriculture ($110,000). This project will be conducted through a contract because the necessary expertise and staff are not available inhouse.

4. Project Monitor/Contact:

Dr. Helen Hofer Gee
Program Evaluation Branch, OPPE/OD/NIH
Building 1, Room 228
(301) 496-4418

5. Coordination:

This project will be reviewed by the NIH Evaluation Oversight and Policy Committee and the NIH Evaluation Technical Review Committee. In addition, there is an ad hoc oversight committee for this project including: Mr. Kurt Habel, Dr. Ruth Kirschstein, Dr. Thomas Malone, Dr. Ed Rall, and Dr. William Raub.

6. Program Evaluated: DHS-NIH-Biomedical Research

This evaluation addresses all programs in NIH concerned with basic research in biology.

7. Intended User:

The primary users will be the Director NIH, BID Directors, Study Sections, and other components of NIH that are concerned with allocating resources among biomedical research programs. For some program managers, this study will identify opportunities for scientific advances that can be achieved only by establishing new links between their programs and other selected disciplines and programs.

8. Information to be Generated:

The primary output will be the identification of scientific opportunities and recommendations for seizing these opportunities in areas of biology including: tropical biology, membrane biology, microbial ecology, animal behavior, neurobiology, evolution and paleontology, development, immunology, virology, soil biology, systematics, and reproductive biology.

9. Approach:

The National Academy of Sciences and National Research Council will establish a Steering Committee and panels of experts in each of the areas of biology selected for the study. Each panel will prepare a report on research opportunities in its area. The Steering Committee will synthesize these reports and develop an integrated set of recommendations.

Attached is a proposal from NAS giving greater detail on the background and approach proposed for this study.

10. Information Clearance/Collection: No

11. Pre-Rule Making Activity: No

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier: NIH 86-301

2. Project Title and Capsule Description: Development of an Inventory of Data Elements in Existing Databases That are Useful for Program Evaluation.

The NIH has developed several large databases that have proved invaluable in program evaluation (e.g. IMPAC, CRISP). Over the last few years, several new databases have become operational (e.g. consolidated grant applicant file, bibliometric files). The primary products of this study will be a) an inventory of those databases that are likely to be useful for program evaluation and b) a consolidated data dictionary of the data elements in these databases. Users of the data dictionary will be referred to the appropriate contacts for alternative databases where particular information resides. The dictionary will also provide basic information on each data element such as definition and period covered. Thus, this study will support development of general evaluation methodology and the initial development of instruments which will be used for program monitoring and evaluation.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	2	2	-
87	3	3	-

This study is an inhouse effort. To facilitate both the development and distribution of the consolidated data dictionary, information will be entered and retrieved from the DCRT mainframe, including the periodic publication of the current version of the data dictionary.

4. Project Monitor/Contact:

Sheldon Fishman
Program Evaluation Branch, OPPE/OD
Building 1, Room 228
9000 Rockville Pike
Bethesda, MD 20205
(301) 496-4418

5. Coordination:

This project will be reviewed and approved by the NIH Evaluation Oversight and Policy Committee and the NIH Evaluation Technical Review Committee. In addition, an ad hoc technical advisory committee will be appointed to review all significant decisions and documents. This group will review the content and format of the consolidated data dictionary and will review the selection of databases to be included.

6. Program Evaluated: PHS-NIH-Biomedical Research The databases to be included in this effort will provide evaluation information on the full range of intramural and extramural biomedical research conducted by NIH.

7. **Intended User**: The products of this study will be used by evaluation officers and program managers during the initial design phases of program evaluations. They will be able to determine what data elements are readily available on existing databases and will be directed to the appropriate sources to gain access to those databases.

8. **Information to be Generated**:

If this study is successful, it will provide information to make many program evaluations more efficient and timely. Evaluators will be able to identify data elements readily available and will be directed to the alternative sources for that information. This study will build on the documentation of individual databases such as Information and Instruction Handbook VI-A: Master Files of IMPAC and the Consolidate Files of Grant Applicants and Trainee Fellows (Evaluation Project, NIH/DRG, 84-301).

9. **Approach**:

This study will be based entirely on secondary data. The major steps are:

1. Identify existing databases with potential use for program evaluation
2. Review documentation
3. Develop and apply selection criteria
4. Design a computerized data dictionary to store and manage the information
5. Design format of the published data dictionary and computer query procedures
6. Pilot test
7. Full-scale implementation
8. Publish a current version of the data dictionary
9. Identify an organization to maintain and update this information on an ongoing basis

10. **Information Clearance/Collection**: No, there is no primary data collection.

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier: NIH 86-302

2. Project Title and Capsule Description: Evaluation of the Applicability of Existing Artificial Intelligence (AI) Tools for the Improved Productivity of Biomedical Research Administration

   NIH and others have supported the development of artificial intellegence systems in biomedicine. While these systems may still be on the frontiers of applicability in difficult medical areas (e.g. differential diagnosis), there is increasing evidence that some of the tools utilized by these systems could aid in selected tasks in research administration. This project will evaluate the applicability of AI tools and related new technologies to improve the productivity of biomedical research administration at NIH. If successful, this project could relieve some of the pressures exerted by increasing demand for administrative and support services, and decreasing personnel resources.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	25	10	15
87	15	15	-
88	20	20	-

   This project is basically an inhouse project. During the first year a small personal services contract may be awarded if NIH does not have sufficient staff time in artificial intelligence. The DCRT charges are for pilot tests of an expert system.

4. Project Monitor/Contact:

   Sheldon Fishman
   Program Evaluation Branch, OPPE/OD
   Building 1, Room 228
   9000 Rockville Pike
   Bethesda, MD 20205
   (301) 496-4418

5. Coordination:

   This project will be reviewed and approved by the NIH Evaluation Oversight and Policy Committee and the NIH Evaluation Technical Review Committee. In addition, the NIH Productivity Committee will review the selection of an administrative or support function that can be facilitated by an AI system.

6. Program Evaluated: PHS-NIH-Biomedical Research

7. Intended User: The first users of the methodology to be developed by this study will be managers of personnel intensive activities whose resources have not kept pace with demands.

8. Information to be Generated:

Resources have already been invested in AI systems in biomedical research. For example, a recent citation analysis found 142 articles on AI systems in medical decision-making. The domain of virtually all these projects are difficult clinical areas in which additional research is required. However, many of the tools that were developed while addressing these difficult problem areas may be adequate to solve the more pedestrian problems of research administration. Unlike conventional computer programs that process data, these systems simultaneously process inference rules and data. Consequently such a system can document the logic used in reaching a recommendation. NIH has the computer hardware and the basic software (PROLOG and LISP) to run AI systems. This study will determine if there are research administration tasks that could be facilitated by AI systems tools running on existing NIH computer hardware.

9. Approach:

Task 1: Selection of an Administrative or Support Function as a Pilot Test.

After consulting with the NIH Productivity Committee, an administrative function for pilot testing will be selected. For example, an AI system could provide computer aided documentation of referral of grants to a study section for review or referral to a BID for funding. Since many applications can be referred to one of several study sections, an AI system could facilitate referral. The system could consider scientific topics, history of previous reviews of a particular application, and potential conflict of interest of institutions (e.g. applicant's institution and reviewers' institution) and produce alternative referrals, with documentation of the logic of each alternative. In this case, Al tools will be used in computer-aided decisions.

Task 2: Document information used and decision criteria.

The criteria and information now used for making decisions in a particular function will be fully documented and analyzed. Subtasks that may be aided by Al tools will be identified. In addition, subtasks that are too difficult to be aided by current technology or the proposed level of effort will be identified.

Task 3: Selection of appropriate AI tools.

It is expected that the choice will be made from existing software at NIH (e.g. PROLOG or LISP) or existing AI framework systems.

Task 4: Pilot Test.

A system will be developed on NIH computers to facilitate an administrative or support function. The pilot will test the feasibility and measure the utility of this computer aide.

10. Information Clearance/Collection: No

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier: NIH/NLM-86-305

2. Project Title and Capsule Description:

   a. Title: Development of Evaluation Methodologies to Assess NLM's Coverage of New Biomedical Literatures.

   b. Capsule Description: Among the ways NLM provides service to health researchers, educators, practitioners and students are to: 1) acquire "in-scope" journal and monograph literature for the NLM collection; and 2) facilitate the biomedical community's identification and retrieval of this literature by announcement in Index Medicus and the MEDLARS databases. The purpose of this project is to design, develop, and test new evaluation methodologies appropriate for assessing the adequacy of these functions for new biomedical literatures. Two suitable test domaines have been identified. They are Medical Informatics and Health Services Research. Each area presents special problems for NLM inasmuch as there is a lack of generally agreed upon definitions of the boundaries and structures of these fields, and as is characteristic of work that is highly interdisciplinary, publications may appear in literatures of other fields not necessarily connected with medicine or health. Adequate coverage of these literatures is important to the constituents and missions of the NIH and PHS.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	$35	--	$35

The budgeted amount is intended to cover expenses associated with the consultative services of leading professional societies who will be called upon to assist in this project.

4. Project Monitor/Contact: Elliot R. Siegel, Ph.D., Special Assistant for Operations Research, Office of Planning and Evaluation, National Library of Medicine, Bldg. 38, Rm. 2S-18, 496-8834; and

   Betsy Humphreys, Deputy Associate Director, Library Operations, National Library of Medicine, Bldg. 38, Rm. 2W-06, 496-6921.

5. Coordination: This project has been reviewed by the following NLM officials; Director, Associate Director for Planning and Evaluation, and Associate Director for Library Operations.

6. Program Evaluated: PHS-NIH-Biomedical Research - Library of Medicine.

7. Intended User: Intended users of the information are the senior management of the National Library of Medicine, the management and staff of the Library's operating divisions, and members of the

evaluation research community who undertake scholarly investigations leading to the development of new evaluation methodologies appropriate for tracking and characterizing the literatures of science and technology.

8. Information to be Generated: It is proposed that NLM undertake an evaluation of the Medical Informatics (MI) literature, utilizing an assessment strategy and methodology that can subsequently be applied to Health Services Research literature and other new subject areas. Evaluation will utilize a streamlined version of the citation analysis techniques originally developed in an earlier study by NLM of the Medical Behavioral Sciences literature (Griffith et al, 1983). In addition, the project will also employ non-quantitative methods such as expert ratings and nominations of influential and frequently used publication sources which will be used to validate and augment the information obtained by citation analysis. A systematic comparison of outcomes using these two distinct methodologies has not been previously done. Research questions to be addressed include the following:

   1. What are the content boundaries and literatures that comprise the field of Medical Informatics?

   2. What journal titles does NLM acquire? Index?

   3. What important journal titles does NLM not acquire?

   . . What proportion of the important literature appears as conference proceedings? Does NLM collect this literature?

   5. How might NLM improve access to the Medical Informatics literature appearing as journal articles? Appearing as conference proceedings papers (e.g., indexing of individual proceedings papers)?

   6. In order to accomplish the above, what policy changes (if any) would be required? Impact on resources?

9. Approach: The proposed work will be carried out as three distinct studies each complementary to the others in terms of information sources utilized and methods employed. (Specific subject matter sources cited below refer to the MI literature; comparable sources will be identified and used in assessing the Health Services Research literature.)

   Study 1. "Analaysis of References Cited in Selected Conference Proceedings and Journals".

   A 10 percent random sample of references cited in approximately 5,600 recent articles published in the MI literature (taken from selected conference proceedings and journals) will be analyzed to determine collection and indexing status by NLM and coverage by other abstracting and indexing services. Other pertinent information necessary to characterize the citations and the publication sources (e.g., date, subject, country of origin, etc.) will be

documented. Vocabulary used to index the literatures will be analyzed. A principal product emerging from the citation analysis will be a ranked list of the most frequently cited (and presumably high-quality) publication sources expressed as titles of journals, conference proceedings and monographs.
Study 2 - "Experts' Ratings and Nominations of Important and High Quality Publications Sources"

A panel of leading MI experts (n<10 persons) designated by the field's major professional society will be asked to provide a working definition of the field and its major subfields. The list of most frequently cited publications identified and ranked in Study 1 will be rated by the panel on such attributes as perceived quality, importance to the field, and frequency of carrying MI pieces. (The source of the list will not be revealed to the experts.) Titles not on the list, and judged by the experts to be of high quality and interest to the MI community, will be nominated and similarly rated. All titles will be characterized in terms of their relation to medicine and health. Significant discrepancies observed within and between the two methods of citation analysis and experts' ratings will be reconciled.

Study 3 - "Experts' Publication Behavior"

As a check on experts' ratings and nominations in Study 2, approximately 20 to 30 persons who are currently active and established researchers in the field of MI will be identified from among the membership lists of MI professional societies, and searches of the Science Citation Index (SCI) and other databases will be conducted for the purpose of identifying where these persons have published during the most recent 5 to 10 year period. Researchers will be selected on the basis of personal reputation and as being broadly representative of the various subfields of MI.

A comparison of outcomes obtained with each of these three evaluation methodologies will be made, as will an assessment of the relative cost-benefits of each for the types of literatures studied.

10. Information Clearance/Collection: No.

11. Prerulemaking Activity: None

12. References:

Griffith, B.C., White, H.D., Drott, M.C. and Saye, J.D. An Analysis of the National Library of Medicine's (NLM) handling of the Medical Behavioral Sciences literatures: Some research tests of methods for evaluating bibliographic databases. NLM-Drexel MBS Project, Executive Summary, Philadelphia, PA.: Drexel University, College of Information Studies, 1983. N01-LM-2-3510.

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier:

NIH/NLM 86-306

2. Project Title and Capsule Description:

a. Title: Evaluation of the scope and coverage of NLM's TOXLINE database.

b. Capsule Description:

The Toxicology Information Program (TIP) at NLM proposes to analyze the qualitative and quantitative dimensions for subject coverage in its TOXLINE (Toxicology Literature Online) file. TOXLINE has a broader subject coverage than the other online databases maintained by the TIP, and, therefore, an evaluation of the scope and coverage of the TOXLINE file can serve as an indicator for how well the Program as a whole is covering the interdisciplinary science of toxicology. However, the specific purpose of this project is to assess the content scope of TOXLINE as it compares to the toxicology of today, and also of tomorrow, and to identify subject areas for enrichment.

An enhanced TOXLINE file will benefit users in both the Federal and non-Federal sectors. Among the high use Governmental agencies are NCI, NIEHS, CDC, FDA, EPA and several state government systems. In view of the widespread utilization of TOXLINE by both Governmental and non-Governmental organizations and by both national and international communities for purposes of research, education, health care and regulatory activities, it is imperative that TOXLINE be maintained as a high quality file in that its subject coverage reflect the current concerns of toxicology and related disciplines.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges	Other Expenditures
'86	$75	--	$75
'87	$30	--	$30

To analyze TOXLINE coverage and compare it to other data bases will require approximately $25,000 in FY'86. Much of the work for this analysis can be performed by in-house staff, but funding is required to pay for access to non-NLM databases. The amount budgeted to identify trends in toxicology research and practice is estimated at $50,000 for FY'86 and $30,000 in FY'87. The funding will support an advisory committee to oversee the final phase of the project, computer charges, and contractual activities necessary to identify newly emerging areas of toxicological research.

4. Project Monitor/Contact

Dr. Henry M. Kissman
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Specialized Information Services
National Library of Medicine
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Telephone: 301/496-3147

and

Dr. Dorothy Stroup
Technical Information Specialist
Specialized Information Services
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Bethesda, MD 20209
Telephone: 301/496-6531

5. Coordination:

This project has been reviewed by the following NLM officials: the Director, the Associate Director for Planning and Evaluation, the Associate Director for Specialized Information Services, and the Special Assistant for Operations Research.

In addition, the project has been endorsed by the Toxicology Information Program Committee, an advisory committee to the Program that functions under the auspices of the National Academy of Sciences.

6. Program Evaluation:

PHS-NIH-Biomedical Research-Library of Medicine

7. Intended User:

Intended users of the information are the senior management of the National Library of Medicine, management and staff of Specialized Information Services, and members of the Toxicology Information Program Committee, an advisory committee to the Program that is operated under the auspices of the National Academy of Sciences.

8. Information to be Generated:

Fundamental changes are now taking place in the biological sciences that will effect changes in the science of toxicology and its information support systems. In order to provide optimal service to its constituent biomedical user community, the NLM's Toxicology Information Program (TIP) must understand these ongoing scientific changes, evaluate the effects such changes will have on information requirements, and prepare for enhancements or additions to TIP services and activities as required.

The TOXLINE database has the broadest subject coverage of the TIP-managed Chemical and Toxicological online files (CHEMLINE, TOXLINE, Registry of Toxic Effects of Chemical Substances, and the Toxicology Data Bank). It is constructed from "toxicology" subsets obtained from the major U.S. secondary services, including Biological Abstracts, Chemical Abstracts, and Index Medicus. The subject scopes of these various subsets were established several years ago and have not changed substantially over time. TOXLINE and its two backfiles contains approximately 1,500,000 bibliographic citations and, cover the relevant literature from 1965 to date. A detailed analysis may show that TOXLINE's emphasis in a particular area is out of proportion with current realities. Of greater concern is the need to identify areas of high current interest, e.g., biotechnology or alternatives to animal testing, where TOXLINE coverage may be weak or deficient. Yet a third area of investigation is to identify newly emerging areas of scientific activity---"tomorrow's toxicology". Once these subject areas have been determined TIP can take the necessary actions to enrich and enhance TOXLINE.

The fundamental questions to be answered are as follows:

1. What are the areas of subject coverage in the current TOXLINE file? How relevant are these to the scientific and societal concerns of the present?

2. How adequately is TOXLINE covering areas of high current interest, such as biotechnology or alternatives to animal testing? What sources can be found to enrich TOXLINE for areas in which it is found lacking?

3. How can newly emerging areas of toxicological research be identified? What sources can be found to enrich TOXLINE for these areas?

9. Approach

The work, as proposed, will divide into three phases. The first two are inter-related, as described below, and the third is an independent study.

a. Description of the present subject content of TOXLINE:

A preliminary analysis of TOXLINE coverage has been accomplished through computer programs developed in-house. The preliminary computer analysis produced an overview of file coverage with a breakdown into rather broad subject areas, e.g., occupational hazards, adverse drug reactions, chemical carcinogenesis, air pollution, etc. The technique needs to be further refined by the selection of more specific keywords or descriptors to delineate discrete subsets of toxicological research and practice. Greater resolution of the technique will be necessary to pinpoint subject areas that may be inadequately covered in TOXLINE and these, once identified, will be tested further as described in the next study.

b. Comparison of TOXLINE coverage with other files:

A detailed analysis of TOXLINE's subject areas will not *per se* indicate whether coverage is adequate or inadequate. Rather, a comparison of subject content and coverage with other databases is needed. Such a comparison should include the secondary services that contribute subfiles to TOXLINE (Biological Abstracts, Chemical Abstracts, Index Medicus, etc.) as well as other relevant databases that might be available on online systems, such as Dialog, SDC and BRS. New technologies and software systems have been developed to facilitate cross-file searching, in particular micro-CSIN and SCIMATE as implemented on personal computers. These technologies permit the same search strategy to be performed against multiple databases from a variety of online systems. For example, the search for the keywords 'BIOTECHNOLOGY or RECOMBINANT DNA or GENETIC ENGINEERING' can easily be performed in step-wise fashion across TOXLINE, MEDLINE, and a number of other, non-NLM databases. Retrieval results can then be captured, analyzed, and compared, and subject coverage among the various databases can then be assessed.

Content areas to be searched and compared across various databases will be identified in the first study. In addition, select areas of high current interest, such as biotechnology, immunotoxicology, or alternatives to animal testing, which have been recommended by the Toxicology Information Program Committee of the National Academy of Sciences, will also be tested. After analysis, it may be relatively straightforward to adjust TOXLINE coverage in certain speciality areas by changing the selection/extraction protocols used to build the TOXLINE subfiles from other major abstracting and indexing databases. For other areas it may be necessary to identify new sources of information for TOXLINE and/or to initiate new activities and services by TIP.

c. Identification of newly emerging areas of toxicological research: (Bibliometric methods for diagramming the structure of science).

This study proposes to use the bibliometric techniques of bibliographic coupling and/or co-citation analysis to identify newly emerging frontiers in toxicology. Both approaches have been used successfully in a variety of scientific domains. (See, for example, the work of Small at the Institute for Scientific Information, Griffith at Drexel University, and Lowe at NIH). These techniques may be automated, and, if proven effective in identifying frontiers of toxicology, they could be readily adapted as ongoing measures of currency and relevancy for the TOXLINE file.

An advisory committee with expertise in toxicology and bibliometrics will be assembled to provide guidance and oversight for the third phase of this project.

10. Information Clearance/Collection

    No

11. Prerulemaking Activity: None

Reviewed and approved by
NIH Committees

1. NIH Evaluation Project Identifier: NIH/NIDR 86-310

2. Project Title and Capsule Description:

   a. Title: Bibliometric Evaluation of Social and Behavioral Science Research in Dentistry

   b. Capsule Description: The publication and citation characteristics of social and behavioral science research in dentistry will be analyzed using existing bibliometric databases. The bibliometric performance of those investigators supported by the NIDR will be compared with a group of investigators who did not receive such support.

3. Cost and Funding Source:

Fiscal Year	Expenditure (in thousands)	DCRT Charges (in thousands)
86	$100	

Justification: The NIDR intends that the project will serve as an initial case study to evaluate the adequacy of existing NIH bibliometric databases for analyzing the characteristics of the social and behavioral science literature generated by investigators supported by the NIH. To ensure that will be the case, the NIDR asked the NIH Health and Behavior Working Group composed of scientists from several BIDs to review the project description for its applicability to other BIDs. After their review, the members of the Group indicated that the project will be broadly useful to Social and Behavioral Science programs throughout the NIH. They also believe the proposed method of analysis can serve a a model for similar studies in other BIDs.

The project will also describe the particular bibliometric characteristics of the social and behavioral science literature related to dentistry and assess the performance of those scientists supported by the NIDR. In particular, the project will assess the extent to which behavioral science research funded by the NIDR has investigated the relationship between health outcomes and social and behavioral variables. The project will be conducted through a contract because the necessary expertise and staff are not available in-house.

4. Project Monitor/Contact:

Dr. L. Jackson Brown
Evaluation Officer
Office of Planning, Evaluation, and Communications
National Institute of Dental Research
Building 31, Room 2C-36
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(301) 496-6705

5. Coordination:

Dr. Harald Löe, Director
Dr. Marie U. Nylen, Associate Director for Extramural Programs
Dr. Lois K. Cohen, Assistant Director, International Health and Chief, Office of Planning, Evaluation, and Communications
Dr. Patricia S. Bryant, Health Science Administrator for Behavioral Research
Dr. Dushanka V. Kleinman, Chief, Planning and Evaluation Section

6. Program Evaluated:

NIDR Behavioral Science Research
PHS-NIH-Biomedical Research-Institute Specific-Dental

7. Intended Users:

a. Primary Users:

Executive Staff, NIDR
HSA in Extramural Program, NIDR
Executive Staff, NIH and other Bid's
Health and Behavior Working Group, NIH

b. Timetable:

1. RFP Developed	December 1985
2. Evaluation Begun	September 1986
3. Final Report	February 1988

8. Information to be Generated:

The primary objective of the project is the development of a bibliometric profile of the social and behavioral science literature related to dentistry. The information on publications and their citations represent a set quantitative measures of the outcomes of dollars and resources expended on social and behavioral research related to dentistry. The contractor will determine which bibliometric databases are necessary to conduct a bibliometric analysis of social and behavioral research relating to dentistry. Those databases that are currently maintained by the NIH will be used when possible, but additional publication and citation information from other sources will be acquired if they are necessary to describe the literature satisfactorily. Then, using bibliometric analysis, the contractor will (1) determine the scope and field of research publications, (2) define the extent and character of collaboration that exists among social scientists themselves and with investigators from other disciplines, and (3) describe the width of utilization of the publications by citation analysis for the social and behavioral science literature related to dentistry. Furthermore, within this literature base, the contractor will develop publication and citation profiles of NIDR-supported investigators. These profiles will be assessed to determine the extent to which behavioral research funded by the NIDR has investigated the relationships between health outcomes and social and behavioral characteristics of individuals. To the extent possible, the bibliometric characteristics of NIDR-funded investigators will be compared with those of similar investigators not funded by the NIDR.

9. Approach:

The NIDR will provide the contractor with a list of social and behavioral science investigators supported by the NIDR and an extensive bibliography of the most important articles in the social and science literature related to dentistry since 1955. The contractor will assess the bibliometric databases currently supported by the NIH to assertain whether a sufficient number of the articles on the list appear in the current databases. If necessary, the contractor will supplement these databases with additional journals and will lease the social science citation index database for the appropriate years.

Using the combined databases, the contractor will describe the salient bibliometric characteristics of the social and behavioral science literature related to dentistry. The description will include a listing of the most important journals for the publication of this literature, the number of publications and the annual publication rates for these investigators, the most important sub-fields in the literature, the citation and co-citation frequency for articles in this literature alone and compared to other areas of the biomedical literature relating to dentistry, and most productive and the most cited investigators working in the area.

The contractor will also compare the publication and citation profiles of investigators who were supported by the NIDR to a comparison group of investigators who were not. These groups will be controlled for the sub-field of the investigation as appropriate. Specifically, the two groups will be compared regarding (1) the journals in which they publish, (2) the number and type of authors, (3) the number and type of institutional affiliation, (4) the number and type of documented support sources, (5) the quantity and frequency of their publications, and (6) the quantity and frequency of citations and co-citations that their articles subquently generated.

10. Information Clearance/Collection: No

11. Prerulemaking Activity: None

UNDER REVIEW

1. NIH Evaluation Project Identifier: NIH/DRR 86-314

2. Project Title and Capsule Description: An Examination of the Issues Surrounding the Use of Laboratory Animals in Biomedical and Behavioral Research. This evaluation will examine the benefits to humans and animals - past, present and future - arising from the use of laboratory animals; will assess developments in science, both current and future, which may serve to reduce the nation's needs for laboratory animals; and will assess public concerns which may lead to further federal legislation and regulatory actions affecting biomedical research.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	$135,000	- - -	- - -
87	- - -	- - -	- - -

The Academy has sought and obtained the broad sponsorship recommended by the NIH. Two-thirds of the total project cost of $405,000 will come from the following sources - NSF ($50,000), DOD ($60,000), USDA ($50,000), and the Pharmaceutical Manufacturers Association ($110,000). NIH's contribution of one-third of the study's costs comes to $135,000.

NIH does not have available sufficient staff to accomplish this study in-house.

4. Project Monitor/Contact:

Dr. James D. Willett
Chief, Biological Models and
Materials Resources Section
Animal Resources Program
Division of Research Resources
Building 31, Room 5B23
9000 Rockville Pike
Bethesda, Maryland 20892
301-496-5175

5. Coordination: This project has been reviewed by the NIH Director, the NIH Evaluation Policy and Oversight Committee, the NIH Technical Review Committee, and an ad hoc advisory committee. This ad hoc committee is comprised of: Dr. William Raub, Deputy Director for Extramural Research and Training (Chairman); Mr. Kurt Habel, Acting Associate Director for Program Planning and Evaluation; Dr. Robert Whitney, Director, Division of Research Services; Dr. Charles McCarthy, Director, Office for Protection from Research Risks; Dr. Betty Pickett, Director, Division of Research Resources; and Mr. Storm Whaley, Associate Director for Communications. This ad hoc advisory committee will provide continuing oversight of this study.

6. Program Evaluated: PHS-NIH-Biomedical Research

This study addresses the full range of NIH's intramural and extramural research programs dependent upon the use of laboratory animals. Such projects account for 44% of NIH's extramural efforts. An evaluation of the benefits to humans and animals derived from research employing animal models, developments in science likely to affect the nation's need for laboratory animals, and public concerns likely to lead to further federal legislation and regulations is needed (useful) to the NIH in explaining the importance of laboratory animals to biomedical research and in sensing and responding to developing changes in where and how animal models are used in biomedical research.

7. Intended User: The results of this study will be used by the Director of NIH in planning research programs and reviewing current policies regarding the use of animals in NIH-supported research. The Assistant Secretary of Health has also expressed to the Director of NIH an interest in the results of this study. This study will also respond to Congressional interests as expressed in S-540 in the 98th Congress, which specifically called for a study of animals in research.

8. Information to be Generated: Phase I of NIH's evaluation of the Uses of Animals in Research began with the study, NIH-DRR85-310, seeking objective data on the nation's use of laboratory animals. Phase II of this evaluation is needed by NIH to aid review of its current policies regarding the uses of animals in biomedical research and is responsive to Congressional interests in the nation's use of laboratory animals. Phase I of this evaluation is supporting the development and test of a means of acquiring objective data on the use of laboratory animal resources within the U.S. A pilot study is underway which will lead to a full-scale national survey of the kinds and numbers of laboratory animals used.

Design and test of the survey instrument and conduct of the national survey, if approved by OMB, are being conducted through the National Academy of Sciences' Institute of Laboratory Animal Resources (ILAR) and coordinated by the Commission of Life Sciences (CLS). Phase II of the study of the Uses of Animal in Research will evaluate issues of broad relevance to the totality of biomedical research and biological testing. As such, the Academy has obtained broad sponsorship for this portion of their proposed undertaking, and NIH will contribute up to one-third of the costs for the Phase II efforts.

Phase II of the proposed NAS Uses of Animals in Research study seeks to evaluate the benefits to humans and animals (past, present and future) arising from the use of laboratory animals and public concerns that may lead to further federal legislation and regulatory actions affecting biomedical research. The study will also provide an assessment of the developments in science, both current and future, that may serve to reduce the needs for laboratory animals.

9. Approach: Information gained from Phase I of the study of the kinds, numbers and purposes of use of laboratory animals in the national research and testing enterprise will serve as background to the NAS committee conducting the proposed evaluation of the issues surrounding the uses of laboratory animals in Phase II.

The issues portion, or Phase II, of the Uses of Laboratory Animals in Research study will gather information on the laws, regulations and policies governing the use of laboratory animals and their implementation at all levels, including that of the individual investigator. This will provide an in-depth analysis of the array of laws, regulations and policies affecting laboratory animal usage at all levels of government (local, state and national).

The benefits accruing to both humans and animals from the use of animals in research will be analyzed and attempts made to identify those steps in key health-related discoveries which were exclusively dependent upon the use of animals.

The Issues Committee will analyze how public concerns over the use of animals in research may affect research dependent upon such use. Effects of current and future advances in science on the use of laboratory animals will be assessed. This will include an examination of past, present and future prospects for developing research methodologies which reduce the research communities need or dependence on laboratory animals.

In addressing the more subjective issues associated with their initial proposal for a study of the Uses of Animals in Research, the National Academy of Sciences has sought and obtained a broadly based sponsorship. This in-depth analysis of the benefits arising from the use of laboratory animals, public concerns likely to lead to further legislation and regulation affecting biological research, and developments in science affecting the needs for laboratory animals has already received support from other federal agencies and the private sector. The Pharmaceutical Manufacturers Association (PMA), the National Science Foundation (NSF), the U.S. Department of Agriculture (USDA), and the Department of Defense (DOD) are helping to finance this study.

The study is administered jointly through the CLS of the National Research Council (NRC) and the Institute of Medicine (IOM). A committee of 13 distinguished individuals with recognized expertise appropriate to this difficult undertaking has been selected (see roster - Attachment 1). Information gained from ILAR's Phase I pilot study which NIH is currently funding, as well as the data obtained from the proposed national survey on laboratory animal use, will aid the issues committee in pursuit of its objectives.

At its first meeting, the issues committee received input from federal agencies and private foundations on the results of prior efforts to address the questions contained in their task (see statement of task - Attachment 2). The Issues Committee is evaluating prior studies pertinent to its task and conducting its own investigations where necessary. Of primary interest to the committee are public concerns over the use of laboratory animals, the extent to which laboratory animals are and have been important to biomedical research, and the present regulatory and policy settings governing the use of animals in research. A review of developments in science affecting animal usage is planned as is an assessment of current alternative methods. Where possible, the committee intends to use data gather in the course of other recent studies whose results are pertinent to their objectives. A report is planned that will make recommendations on the issues of animal use of particular importance to decision-makers, focusing on the concerns of scientists, animal welfare organizations and legislatures.

10. Information Clearance/Collection: No.

11. Pre-Rulemaking: No.

NATIONAL RESEARCH COUNCIL
COMMISSION ON LIFE SCIENCES
2101 Constitution Avenue Washington D C 20418

ATTACHMENT 1

BOARD ON BASIC BIOLOGY

COMMITTEE ON USE OF LABORATORY ANIMALS IN BIOMEDICAL AND BEHAVIORAL RESEARCH*

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*Note: One or two additional members may be appointed

September 26, 1985

Code Designator for Group Described: ____________

Commission on Life Sciences/IOM
ASSEMBLY or COMMISSION

Committee on the Use of Animals in Biomedical and Behavioral Research
COMMITTEE

DIVISION, OFFICE, or BOARD

SUB-UNIT

Staff Officer: John E. Burris

STATEMENT OF TASK

(Make clear what is expected of the group described. Include any contractual obligation under which the group bears responsibility. Limit to not more than this page.)

The Committee on the Use of Animals in Biomedical and Behavioral Research will be jointly administered by the CLS and the IOM. Major support for this project derives from NIH with the expected participation of NSF, USDA, DOD, other federal agencies, and the private sector.

The task of the committee will be to examine the use of animals in laboratory research. Public concerns about animal use and treatment, benefits derived by humans and animals from research with animals, and the scientific and technical developments that may affect the use of animals for experimental purposes will be addressed. The committee will also assess the effectiveness of current regulatory and self-regulatory or voluntary guidelines for animal care and use. The above task will be accomplished using findings of the committee coupled with a survey being concurrently conducted by an Institute of Laboratory Animal Resources committee.

The products of the committee work will appear in a report to be published two years after the inception of the effort.

August 21, 1985

FY 85 Project Approved
but not previously
included in Plan

1. NIH Evaluation Project Identifier: NIH/NICHD 85-312

2. Project Title and Capsule Description:

   a. Title: Matched Comparison Evaluation of NICHD Intramural Research Publications Using Biomedical Science Clusters

   b. Capsule Description: We seek to explore the utility of developing objective methods for appraising publications by NICHD intramural scientists. The study will comprise two parts 1) Locating NICHD intramural publications for 1982 within the biomedical clusters developed by the Institute for Scientific Information (ISI). Where no dominant clusters exist "synthetic clusters" will be derived by bibliographic coupling; 2) Evaluate the appearance of NICHD intramural publications among bibliographic citations and compare these citation counts with those characteristic of non-NICHD publications falling in the same clusters. When intramural publications do not appear in a dominant cluster, matching non-NICHD publications will be found through bibliographic coupling used to produce "synthetic clusters".

3. Cost and Funding Source:

Fiscal Year	Expenditure (in thousands)	DCRT Charges (in thousands)
1985	$14	
1986	$ 6	

Funding is requested from one percent set-aside funds. This study could serve as a model for gaining added perspective on the intramural programs of other Institutes if citation and co-citation methodology were applied to appropriate annual publication sets. The $20,000 will be used for the labor and non-labor costs at ISI to extract the data and analyse the results using publications from the year 1982 as the primary input data.

4. Project Monitor/Contact: Dr. Charles U. Lowe, NICHD, Building 31, Room 2A20, 496-2500; Dr. Arthur S. Levine, NICHD, Building 31, Room 2A50, 496-2133.

5. Coordination: This project has been reviewed and endorsed by the following committees: the NIH Evaluation Oversight Committee, the NIH Technical Review Committee, the Board of Scientific Counselors of NICHD. As the project proceeds, a standing committee with expertise in bibliometrics will review and assist in evaluating the results. (See appendix for list of members of Review Committee)

6. Program Evaluated: NICHD Intramural Program

7. Intended Users: Scientific Director, NICHD; Director, NICHD; and potentially other NIH Scientific Directors and Institute Directors

8. Information to be Generated: In this project we propose to explore a form of literature analysis as one objective tool and an additional perspective for reviewing of the NICHD Intramural Program. The first phase of this project will locate the 1982 NICHD intramural publications, as citing (source) articles, in the 1982 biomedical co-citation clusters regularly generated by ISI on an annual basis. (These science clusters group citing articles based on use of common references.) The clusters can be thought of as research fronts nominally identified by a group of citing articles. Once the intramural publications are located in a science cluster, matching non-intramural publications can be found in the same cluster. These non-intramural publication will contain references in common with the intramural articles and focus on the same subject area. The non-intramural publications will be used as comparison groups for the citation study in Phase II.

Several additional indicators will be compiled, by cluster, during Phase I. These indicators concern the distribution of NICHD intramural publications across different research areas and the relative concentration of the NICHD articles within specific research areas. These indicators include: 1) The proportion of the total NICHD intramural effort that is concentrated in any research front. Independent of the size of the research area, does a high proportion of the total NICHD intramural effort concentrate in a few research areas, or is it distributed over many areas; 2) The degree to which the research areas that the intramural program participates in are "dominant" (i.e., popular areas, with a large number of publications produced relative to other areas), "nondominant" or "synthetic".

The second phase will generate the citation levels of the 1982 intramural articles in 1983 and 1984. These citation levels will be compared against a matched set of non-intramural 1982 articles that were located in the 1982 clusters where intramural publications appeared. Aggregate quality measures will be calculated for the intramural and comparison groups (citations divided by number of publications). Since this kind of a matched comparison controls for the size of subject area, it will assess relative citation performance more accurately than counts based on journals (or sets of journals) that encompass a range of subject areas. This measure is a preliminary profile of the aggregate quality of the intramural program relative to other research in the same area as judged by peer citation. Quality measures of 1982 publications based on the 1983-1984 period remain tentative since citation counts typically peak three to four years after publication. However, the ordinal ranking of intramural versus non-intramural aggregates in various subject areas should not vary much between the 1983-1984 and 1985-1986 periods because a large proportion of citations are typically generated within three years of publication.

9. Approach: In Phase I, a list of all the 1982 NICHD intramural publications will be obtained from the Scientific Director, NICHD. These publications will be keyed to a tape in the citing article format used by ISI. The articles will then be matched against the 1982 ISI biomedical co-citation clusters. Output files will be generated containing the comparison publication data and intramural participation measures will be calculated. For intramural publications that are not located in an ISI cluster, bibliographic coupling will be used to identify a comparison group creating "synthetic clusters". The size of reference lists and number of matching references will be used in defining criteria for the comparison group.

   In Phase II we will match the intramural publications and the comparison publications against the ISI citation data base for 1983 and 1984 in order to generate citation measures for the intramural and non-intramural publications. Software will be coded to carry out the above tasks.

10. Information Clearance/Collection: None

Advisory Committee

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FY 85 Project Approved
but not previously
included in Plan

1. NIH Evaluation Project Identifier

NIH/CC 85 - 314

2. Project Title and Capsule Description

a. Preliminary Assessment for a Study of Patient Classification System Alternatives in the NIH Clinical Center.

b. The Patient Classification System in the NIH Clinical Center will be critically examined toward the future goal of modifying it. This assessment represents the first phase in a three-phase process which will review nursing productivity in the Clinical Center. In this first phase, consultation from experts in the field is sought to determine if changes in the CC Patient Classification System would make it more effective. (The relationship of patient classification to nurse staffing, workload and productivity is well established. Considerable literature exists which supports and explains this relationship).

3. Cost and Funding Source

Fiscal Year	Expenditures (In thousands)	DCRT Charges
1985	$ 4	---
1986	$21	---

This cost will cover the fees of three national experts in the Patient Classification field who will be brought in to counsel and advise the Nursing Productivity Committee established by the Clinical Center Director. This consultation will afford guidance in the shaping of a future study of nursing productivity with emphasis on examination and change of the Patient Classification System.

4. Project Monitor/Contact

Dr. Margaret Dear
Room 2C-206, Clinical Center
496-5661

5. Coordination: Rena Murtha, R.N., M.A., Associate Director, CC, for Nursing, has reviewed this project. Continuing coordination of this phase with subsequent phases is being provided by the ad hoc Nursing Productivity Committee appointed by Dr. John Decker, Director, Clinical Center. The Committee includes representatives from nursing and management.

6. Program Evaluated

PHS - NIH - NURS - CC - Patient Classification System

7. Intended User

The information generated will be used by the Director of the NIH Clinical Center. The Nursing Productivity Committee, established by the Director of the Clinical Center, will benefit from the insight gained into alternatives to the present Patient Classification System.

8. Information to be Generated

The intensive consultation made available to the Clinical Center Nursing Productivity Committee will be provided over a three to four month period beginning 5/85. It will assist the Committee in answering the following questions:

a. How appropriate is the present Patient Classification System in determining the staffing pattern for nursing in the inpatient and outpatient areas of the Clinical Center?

b. Given the unique nature of the Clinical Center and its biomedical research mission, what features and attributes of the current Patient Classification System must be changed in order to reflect newer protocols and expanded demand for nursing in the Clinical Center, including the recently completed Ambulatory Care Research Facility?

c. If it is determined that it is feasible to carry out a major study and modification of the Patient Classification System, what are reasonable estimates of amounts and kinds of resources required and necessary steps to be taken?

Consultants will meet with the Nursing Productivity Committee to discuss the Patient Classification System currently in place in the Clinical Center. Consultants will have the opportunity for meetings with other Clinical Center personnel as needed to accomplish the task of reviewing the patient classification system.

9. Approach

In line with widespread interest in the topic, the Clinical Center plans to estimate the level of nursing productivity within the Department of Nursing in Phase II and III of the planned project. The timeliness of such evaluation is especially appropriate given the expansion of Ambulatory Care and generally increased demand for nursing services. An integral part of productivity is nurse staffing to achieve desired outcomes. Nurse staffing and workload are based on patient classification systems which may vary in type from institution to institution.

Considerable work has already been done in the area of patient classification in other hospital settings. However, measures remain somewhat crude and there is no single patient classification system which has achieved general acceptance in all hospitals. The NIH Clinical Center is unique, and the problem of refinement of the patient classification system is evident here. The nature of the Clinical Center and its research mission add unusual dimensions to the nursing responsibilities. Nursing output, difficult to measure at best, becomes more complex in the presence of the research-related functions of nursing staff as well as the needs of persons who are patients and research subjects.

Thus the planning of a study is more difficult in the NIH Clinical Center than in typical hospital settings. The shaping and direction of Phases II and III of the project are critically important. It is apparent that a patient classification system used in a general hospital setting may not be transferrable here. An appropriate patient classification system must be functional before an assessment of nursing productivity (Phase III of the project) can be begun.

A Nursing Productivity Committee has been formed by the Clinical Center Director with representatives from nursing and management. While the group contains a range of expertise and experience with both patient classification systems, hospital management, data management and nursing, input from experts in the patient classification field is essential to the Committee as it initiates and guides the progress of study development.

Such consultation rendered over an intense period of performance in Phase I will allow the Committee to move to the second step: a quantitative in-place assessment of the relative utility of the current and proposed alternative systems of patient classification (Phase II). The evaluative project would thus be developed with input from top expertise in the field combined with the strengths already present in the Committee.

Specifically, the consultants will be selected on the basis of their expertise in Patient Classification Systems and will be asked to deliver the following:

1. a report from each of the consultants responding to the questions formulated in Section 8.
2. from the most senior consultant, a synthesis of the individual findings to show the areas of agreement and options open to the Nursing Productivity Committee and its Chairman.
3. an assessment of the CC patient classification system and recommendations for change.
4. a seminar in which consultative findings might be presented and discussed with the Nursing Productivity Committee.

The consultants will provide an outside group view of the Clinical Center Patient Classification System as well as three individualized perspectives. At the end of the consultative period, they will thus provide a consolidated statement of work for the two subsequent phases of the project. During Phase II of the project, this statement of work will be used to establish a fair Patient Classification System at the Clinical Center; during Phase III a full evaluation of nursing output will be carried out in the light of the modified Patient Classification System.

10. Information Clearance/Collection:

No

FY 85 Project Approv
but not previously
included in Plan

1. NIH Evaluation Project Identifier: NIH/DRG 85-315

2. Project Title and Capsule Description:

   a. Title: Improvement of Information about Earned Degrees of Grant Applicants

   b. Capsule Description: This project will gather data from grant application files to make corrections and to standardize the way in which degrees of NIH grant applicants are stored in the IMPAC system. The information on degrees is important in following trends of employment of MDs and other health professionals as principal investigators on NIH research grants and in the planning and evaluation of training grant programs and other initiatives to encourage the entry of clinicians into research careers.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)
86	$50

Justification:

Preliminary sampling of the computerized files and comparison with study section records for FY 1983 indicated a higher than acceptable rate of error, particularly for applicants who have more than one doctorate. Although corrective action has been taken to record accurate information currently and in the future, there is evidence of inaccuracies for several years after FY 1980. An outside service contracting organization is needed to compare the computer-generated lists with hard copy files in order to make corrections where needed on the lists. Some of the information will be difficult to find because some applications will be in storage, and others may be in boxes awaiting shipment to storage.

Much of the work producing lists of applicants, grant application numbers, and existing degree information in IMPAC; and correcting, matching, and updating IMPAC records in those cases where the contractor finds errors will be conducted in-house.

4. Project Monitor/Contact:

Dr. John C. James
NIH, Division of Research Grants
457 Westwood Building
Bethesda, MD 20205
301-496-7554

5. Coordination: DRG ad hoc Committee on Applicant Degrees, NIH ADP Coordinating Committee, and NIH, OPPE, Program Evaluation Branch

6. Program Evaluated: Kinds of manpower on NIH research grant and training programs as reflected by the degrees of applicants.

7. Intended User: OPPE and training program officials throughout NIH, and others having a need for more accurate information about degrees of NIH grant applicants. The improved information will be very important to managers and directors making policy decisions

regarding efforts to attract MDs into research.

8. Information to be Generated: This project will produce corrected and updated information in IMPAC item #10 covering approximately six or seven fiscal years during the period FY 1980-1986.

9. Approach: Initial efforts will be focused on earlier records before such records are destroyed. Lists of first time ever applicants will be generated by DRG from the Consolidated Grant Applicant File (CGAF) for the use of a data services contractor. The contractor's source of hard copy files will be the Institutes' grant file rooms and/or records sent to Suitland, Maryland for storage. The Evaluation Project generated files containing corrections will be linked to other IMPAC system records in which matches can be made in order to reduce manual processing as much as possible. Plans have been made to expand the size of the degrees item (item #10 in IMPAC) from 8 bytes to 12 bytes to accomodate more information on multiple degrees.

10. Information Clearance/Collection: No

Project No.: NIH 81-302

1. EDC ID No.: 2098

2. Entry Dates:

3. Status: In Process

4. Project Title: Evaluation of the Present Strategy for Dissemination of Consensus Development Statements and of the Impact of the Consensus Development Program on the Practice of Medicine. (Impact Study)

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD-OMAR

7. Start/End Dates: 81/04, 86/02

8. Performer: Rand Corporation, 1700 Main Street, Santa Monica, CA 90406

9. Agency Contact: Dr. Itzhak Jacoby, NIH, Building 1, Room 216
(301) 496-1143

10. Cost: FY 81-$10; FY 82-$418, FY 83-$294, FY 84-$472, FY 85-$7

11. Fund Source: Evaluation

12. Mechanism: Contract

13. Project No.: NIH 81-302

14. Contract No.: N01-OD-2-2128

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research, Office of the Director

18. Evaluation Type: Program Performance Evaluations

19. Descriptors: Medical Practice, Medical Technology, Technology Assessment and Transfer

20. Abstract: This evaluation study will encompass the development of a diffusion model, describing the knowledge transfer process among physicians; the identification of the impact of the consensus development statements arising from Consensus Development Conferences; and the development of an evaluation system for monitoring the technology transfer arising from future conferences. The specific goals of this evaluation of the dissemination of consensus development statements will be to analyze the consensus statements for content; to trace the process by which conference conclusions have disseminated to medical and research communities and to the public; to assess physician's knowledge and attitudes concerning selected medical technologies that have been topics of recent conference, awareness of conference findings; to measure changes over time in hospital practices; and to identify other sources of information about the selected technologies and measure the relative importance of various information sources.

Initial results indicate that the objective of the study will be met.

1. EDC ID No.: 2100 Project No.: NIH 82-302

2. Entry Dates: 3. Status: In Process

4. Project Title: Evaluation of Research Manpower and Training Activities

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 82/05,86/05

8. Performer: Program Evaluation Branch, OPPE/OD/NIH

9. Agency Contact: Dr. Helen Hofer Gee, OPPE/OD/NIH, Building 1, Room 228
(301) 496-4418

10. Cost: FY 82-$30, FY 83-$3, FY 84-$76, FY 85-$64 FY 86-$10

11. Fund Source: Evaluation 12. Mechanism: In house

13. Project No.: NIH 82-302 14. Contract No.: NA

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Program(s) Evaluated: X-PHS-NIH-Biomedical Research-Activity-Training

18. Evaluation Type: Program Strategy

19. Descriptors: Health Manpower Training, Feasibility Study Feature, Research and Evaluation Performance

20. Abstract: In recent years three committees charged with oversight of evalaution in the manpower and training area have each arrived at the same conclusion, namely that there is a need for a full-time concentrated effort to summarize all past evaluation and resource development activities in this area, and to formulate a comprehensive plan for future evaluation studies and other manpower and training information needs.

It is the purpose of this project to implement these recommendations. Specifically, the project aims to (1) summarize all previous evaluation information and survey data on the functioning of NIH training programs; (2) review, interpret, and evaluate all available information on the development of bioscience research careers; (3) determine the adequacy and utility of continuing periodic manpower surveys; (4) conduct a feasibility study of the development of a dynamic flow model of research manpower; (5) conduct minor studies needed to increase the potential utility of a model; and (6) determine the need for future evaluations of manpower and training issues.

Project No.: NIH 83-301

1. EDC ID No.: 2135

2. Entry Dates:

3. Status: In Process

4. Project Title: Evaluation of Biomedical Research Publication Performance

5. Report Title: Various

6. Agency Sponsor: PHS-NIH-OD

7. Start/End Dates: 83-09, 87-09

8. Performer: Computer Horizons Inc. 1060 Kings Highway North Cherry Hill, New Jersey 08034, Mr. Fran Narin

9. Agency Contact: Dr. Helen H. Gee, NIH, Building 1, Room 228; (301) 496-4418

10. Cost: FY 83-$150 (NIH Set-Aside); FY 84-$245 ($97 NIH Set-Aside, $100 NIMH Set-Aside, $48 NIDR Set-Aside); FY 85-$440 ($215 NIH Set-Aside $100 NIMH Set-Aside, $125 NIH General Expense); FY 86-$157 (NIH General Expense); FY 87-$132 (NIH General Expense)

11. Fund Source: Evaluation

12. Mechanism: Contract

13. Project No.: NIH 83-301

14. Contract No.: N01-OD-1-2109 & N01-OD-5-2118

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research - Activity - Research Grants and Contracts

18. Evaluation Type: Methodology Program Effectiveness

19. Descriptors: Biomedical Research Program Coordination, Research and Evaluation Methods Feature

20. Abstract: Revised and expanded methods of analyzing U.S. and foreign biomedical research publications are being developed. Beginning with 1981 data the biomedical publications data base (formerly a 270 journal set) is developed from the National Library of Medicine's MEDLINE System of approximately 3,000 journals. Acknowledgments of research support are indexed. In addition, the data base includes descriptive index terms (MeSH headings). The data are used in evaluation studies of research and training programs and in studies of the impact of policy changes on research productivity. Longitudinal reports on the productivity and influence of each Institute's supported research for FY 81-83 will be available in June 1985. Special studies of National Institute of Dental Research programs were completed in FY 84. Comprehensive information about Federal support of behavioral research is being added to the data bases through NIMH collaboration. Bibliometric data bases are currently being used in studies of post doctoral training, of the Research Career Development program, of Aging Institute programs, and of NHLBI Centers programs.

Beginning in FY 86 effective and economic paradigms will be further developed for bibliometric studies of NIH-defined program areas; reports will be produced for NIH as a whole, for the NIH Intramural program, and for each bureau, Institute and Division (BID), of trends in the quantity and influence of biomedical research publications in relation to funding, for the period 1983-1985. This will extend the previously developed trend data for 1970-1980 in 270 journals, and for 1981-1982 in the larger set of 3,000 or so MEDLINE journals, to include 1983, 1984, and 1985. Studies of the impact of policies on the production of researcn journal papers will be persued.

1. EDC ID No.: Project No.: NIH 83-302

2. Entry Dates: 3. Status: In Process

4. Project Title: An Evaluation of the Impact of RCDAs on the Recipients of the Awards

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 83-05,86-10

8. Performer: Rand Corporation; 1700 Main Street; Santa Monica CA 90406

9. Agency Contact: Dr. Charles R. Sherman; NIH - Building 1 - Room 228

10. Cost: FY 83-$2; FY 84-$142; FY 85-$165

11. Fund Source: Evaluation 12. Mechanism: In house and Contract

13. Project No.: NIH 83-302 14. Contract No.: N01-OD-4-2112

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Impact Evaluation

19. Descriptors: Biomedical Research, Career Development

20. Abstract: The NIH Research Career Development Award is a special salary grant award to support the conduct of research by individuals with high potential for biomedical or behavioral research careers. Over the last 20 years, NIH has provided about 20,000 awards and spent $500M on this program.

The purpose of this study is to assess the professional development of people who have received RCDAs and to compare their progress with that of other bioscientists who have not received RCDAs but are matched on relevant dimensions. Specifically this research will investigate whether the career development of awardees is faster than, the same as, or slower than matched groups of professionals who did not receive RCDAs; assess other aspects of career development, such as breadth of research contributions; and evaluate the results of these assessments relative to program costs.

Project No. NIH/FIC 83-302

1. EDC ID No.: 2134

2. Entry Dates:

3. Status: Complete

4. Project Title: Evaluation of U.S.-U.S.S.R. Individual Health Scientist Exchange Program

5. Report Title: U.S.-U.S.S.R. Individual Health Scientist Exchange (IHSE) Program

6. Agency Sponsor: PHS-NIH/FIC-OD

7. Start/End Dates: 83-9, 85-6

8. Performer: Policy Analysis, Inc.
Brookline, Massachusetts

9. Agency Contact: Coralie Farlee, Ph.D.
Fogarty International Center
Building 38A, Room 605
301-496-1491

10. Cost: FY 83-$45 FY 84-$81

11. Fund Source: Evaluation

12. Mechanism: Contract

13. Project No.: NIH/FIC 83-302

14. Contract: N01-TW-3-2118

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-U.S.-U.S.S.R. Individual Health Scientist Exchange Program

18. Evaluation Type: Program Impact Study

19. Descriptors: International issues, scientific manpower, international collaborative, biomedical research training

20. Abstract: This project report provides an overview of the background, exchange philosophy, program history and current operations of the U.S.-U.S.S.R. Individual Health Scientist Exchange Program. A summary is also provided of the home and host institutions, areas of specialization, length of stay and other data on program participants, as well as commentary on Soviet biomedical institutions and an assessment of the program's administration and management. Recommendations are provided for future program management. Summary findings will be available to future participants and to PHS agencies participating in the program.

1. EDC ID No.: 2131 Project No.: NIH 83-309

2. Entry Dates: 3. Status: Complete

4. Project Title: Study of the Organizational Structure of the NIH

5. Report Title: Responding to Health Needs and Scientific Opportunity: The Organizational Structure of the National Institutes of Health

6. Agency Sponsor: NIH-OD 7. Start/End Dates: 83-04,85-02

8. Performer: National Academy of Sciences, Institute of Medicine
2101 Constitution Avenue, NW
Washington, D.C. 20418

9. Agency Contact: Kurt Habel, NIH, Building 1, Room 228
(301) 496-1454

10. Cost: FY 83-$400, FY 84-$392

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIH 83-309 14. Contract No.: N01-OD-3-2105

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Program Strategy

19. Descriptors: Research and Evaluation Planning and Administration, Research and Evaluation Performance, Research and Evaluation Methods Feature, Reorganization.

20. Abstract: The purpose of the study was to establish the criteria (standards) to be met for determining the need to change, in any substantial manner, the organizational structure of the NIH.

The study included: (a) an analysis of the agency's organizational evolution, those factors contributing to past organizational changes, and the rationale underlying the existing organizational structure; (b) an analysis of approaches to major areas of research which cut across organizational lines, basis for current approaches, alternative approaches for consideration, rationale and implication within current NIH structure; and (c) rationale and criteria to guide further change in the implications such proposed criteria will have on the existing organizational structure.

The study has been completed and the final report was delivered in October 1984.

1. EDC ID No.: 2381 Project No.: NIH/DRR 83-310

2. Entry Dates: 3. Status: Completed

4. Project Title: Model Systems for Biomedical Research

5. Report Title: Models for Biomedical Research: A New Perspective

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 83-08,85-03

8. Performer: National Academy of Sciences
2101 Constitution Avenue, N.W.
Washington, DC 20418

9. Agency Contact: James D. Willett, Ph.D.
Building 31, Room 5B23
(301) 496-5175

10. Cost: FY 83-$150; FY 84-$250

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIH 83-310 14. Contract No.: NO1-RR-3-2112

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research, Research and Evaluation and Administration

20. Abstract: The study of, "Models for Biomedical Research," was an evaluation of the opportunities for and limitations to the use of lower organisms, in vitro systems and nonbiological approaches in developing models for biomedical research. It provides a thoughtful analysis of modeling in the biological sciences. The charge to the Academy committee conducting the study was to: assemble, review, evaluate and report on the relevance of various models for biomedical research. Using a case study approach, five workshops were held sampling the spectrum of biomedical research modeling in cellular immunology,

regulation, learning, diseases and aging, and development. A sixth workshop examined mathematical modeling in biomedical research. The workshops produced insights into modeling and information transfer in biological research that provided a conceptual framework for selection and use of models. In the course of the study a new concept of modeling in biological sciences emerged, i.e., "many-to-many," an approach that compliments modeling by direct analogy, one-to-one, as used in the physical sciences. "Many-to-many" modeling derives analogs to biological structures and functions from the homology of evolutionary relationships. The study makes eight recommendations to the National Institutes of Health regarding modeling and model development in biological research: (1) Support good research without taxonomic or phylogenetic bias and include comparative and phylogenetic studies; (2) Strive to make favorable systems available to the research community by: providing support to supply organisms for research, maintaining stock centers for mutant strains and cell lines, facilitating access to computer programs for biological modeling, maintaining data bases like those for protein and DNA sequences, providing long term support for collections of cloned genes and useful vectors or collections of monoclonal antibodies; (3) Continue to support mammalian models and the search for additional mammalian models; (4) Consider supporting development of new model systems for specific research areas; (5) Consider developing a clearinghouse to encourage the use fo nonmammalian systems for testing the effects of exposure to chemicals of interest to environmental toxicologists; (6) Consider encouraging interest in nonmammalian system through fellowships, symposia, and direct support of model development; (7) Leave the selection of the best system or organism for proposed research to the individual investigator; (8) Investigate the matrix of biological knowledge concept as a potential tool for biomedical research. The NIH received the studies' report, which provides a solid foundation for further development of models for biomedical research, with interest and enthusiasm. Wide dissemination of the studies results are planned. The National Academy of Sciences is marketing the report, and over 300 copies have been circulated throughout the NIH, to select NIH advisory bodies, other Federal agencies, the concerned public, and members of Congress. In the House Report on the Health Research Extension Act of 1985, the Committee on Energy and Commerce, notes the studies results as of potential use to the Director of the NIH in developing and implementing the congressionally directed plan for research on research methods which do not require the use of animals.

1. EDC ID No.: 2382 Project No.: NIH 83-311

2. Entry Dates: 3. Status: Complete

4. Project Title: Evaluation of Biomedical Research Instrumentation in the U.S.

5. Report Title: Academic Research Equipment and Equipment Needs in the Biological and Medical Sciences

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 83-09,85-C6

8. Performer: Westat, Inc.; 1650 Research Boulevard; Rockville, MD 20850

9. Agency Contact: Dr. Charles Sherman; NIH, Building 1, Room 228
(301) 496-4418

10. Cost: FY 83-$50; FY 84-$150

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIH 83-311 14. Contract No.: NO1-OD-3-2120

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research Instrumentation
PHS-NIH-NIGMS Shared Instrumentation Program
PHS-NIH-DRR Biomedical Research Support/Shared Instrumentation Program

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research, Research and Evaluation Performance

20. Abstract: This study evaluates the status of academic research instruments (age, condition, capabilities, usage, etc.) and instrumentation needs in U.S. medical and graduate school laboratories of the biological sciences. The study provides data directly comparable to and contemporaneous with a larger study supported by NSF which examines the same questions in other academic science fields. The results provide guidance for the size and scope of NIH instrumentation support programs, especially in DRR and NIGMS. The stratified samples of 24 medical schools and 42 universities are representative of 92 U.S. medical schools and 157 universities engaged in extensive biomedical research and development.

The survey was begun in March 1984. Questionnaire forms were completed by 367 department chairmen (95% of all surveyed) and by the principal users of 4,397 research instruments (97% of those sampled) valued between $10,000 and $1 million. The results show the 1983 national stock of bioscience equipment in academic settings to have cost $555 million and to be valued at $863 million (replacement cost in 1982 dollars). The average cost was $27,000 per instrument. Only 18 percent of the equipment in use is state-of-the art, and half are in some disrepair. Facilities for maintainence and repair are frequently insufficient. The most urgently needed pieces of equipment appear to be those costing $30,000 or less. In general, the status of research instrumentation in private schools is better than in public schools, and laboratories in medical schools are better equipped than those in graduate schools.

Project No.: PHS/NIH 83-313

1. EDC ID No.: 2385

2. Entry Dates: 3.Status: Complete

4. Project Title: Evaluation of Radioepidemiologic Tables (Radiation-Induced Cancers)

5. Report Title: 1) Assigned Share for Radiation as a Cause of Cancer; 2) Report of the National Institutes of Health Ad Hoc Working Group to Develop Radioepidemiological Tables

6. Agency Sponsor: PHS-NIH-OD 7.Start/End Dates: 83-07, 85-01

8. Performer: National Academy of Sciences, 2101 Constitution Ave., N.W.
Wasnington, DC 20418

9. Agency Contact: Dr. Philip S. Cnen, Jr., NIH, Shannon Bldg., Room 101; 496-3561

10. Cost: FY 83-$90, FY 84-$109, FY 85- $21

11. Fund Source: Evaluation 12.Mechanism: Contract

13. Project No.: PHS/NIH 83-313 14.Contract No.: N01-OD-3-2113

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Cancer

18. Evaluation Type: Other

19. Descriptors: Cancer, Epidemiologic Research, Genetics, Morbidity and Mortality, Statistical Analysis Methods Feature, Statistical Data Feature

20. Abstract: Section 7(b) of the Orphan Drug Act, Public Law 97-414, directed the Secretary of Health and Human Services to develop radioepidemiologic tables that show the probabilities that human cancers are caused by prior doses of radiation. The Secretary delegated the responsibility to the Assistant Secretary for Health, who directed that the study be carried out by an ad hoc Working Group to Develop Radioepidemiological Tables in tne National Institutes of Health. The Assistant Secretary later asked the National Research Council (NRC) to review the data sources, assumptions, methods, and means of handling uncertainty that the Working Group proposed. Tnis evaluation project supported the activities of the 10 member Oversight Committee on Radioepidemiologic Tables (OCRET), which provided an interim report* covering an early draft (July, 1984) of the Working Group's report and submitted a final report** covering the Working Group's draft final report.*** The subjects addressed in these reports include: formulation of the idea of assigned share of risk and its calculus, methods for smoothing

and extrapolating risk estimates over time, methods for projecting risk estimates from one population to another, methods for adjusting risk estimates at low doses and low dose rates or for high-LET radiation, choice of organ and tissue sites for which to produce estimates of assigned share, sources of data on radiation risks, nature and presentation of uncertainties, and other issues.

The final report was issued in December, 1984, and released to the Congress and the public. It includes 25 specific recommendations about data sources, assumptions, methods, and uncertainties. In addition, the report discusses some supplementary economic, social, and ethical issues which aim to alert about possible unintended consequences, as well as problems with the current state of knowledge. The latter include implications for existing radiation protection standards and compensation formulas and systems.

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*Report is entitled, "Assigned Share for Radiation as a Cause of Cancer--Review of Assumption and Methods for Radioepidemiologic Tables".

**Report is entitled, "Assinged Share of Radiation as a Cause of Cancer--Review of Radioepidemiologic Tables Assigning Probabilities of Causation", December, 1984

***The Final Report is entitled, "Report of the National Institutes of Health ad hoc Working Group to Develop Radioepidemiological Tables"; January 4, 1985

1. EDC ID No.: Project No.: NIH 84-301

2. Entry Dates: 3. Status: In Process

4. Project Title: Evaluation of the NIH Small Business Innovative Research (SBIR) Program

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 84-10,89-12

8. Performer: In-house and Contractor (NYD)

9. Agency Contact: Sheldon Fishman; NIH, Building 1, Room 228; 9000 Rockville Pike, Bethesda, MD 20205 - (301) 496-4418

10. Cost: FY85 - $0, FY86 - $80, FY87 - $80, FY88 - $200

11. Fund Source: Evaluation 12. Mechanism: In-house and Contract

13. Project No.: NIH 84-301 14. Contract No.: NYD

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research, Grant and Contract Management

20. Abstract: The Small Business Innovation Research (SBIR) program is comprised of projects in three specified phases:

Phase 1	Grants to establish the technical merit and feasibility of proposed research which may lead to commercial products and services;
Phase 2	Grants to provide support for in-depth development of those research projects conducted under the earlier phase which are most likely to result in commercialization; and
Phase 3	Private capital to develop commercial applications of the results of the federally funded research.

In FY 1983 NIH reviewed 598 phase I applications, awarded 123 grants for $6.5 million, and in FY 1984 reviewed 785 applications (701 for phase I and 84 for phase II) for $21 million. This program evaluation will address effectiveness of implementation, impact, cost of SBIR program, quality of SBIR grants and secondary effects on academic centers and small businesses. In-house activities to date have centered on pilot studies (e.g. correlation analyses of priority scores and cluster analyses of keywords), establishing information files, developing potential comparison groups (e.g. small grants program, new investigator, or first time applicants), and producing annual reports required by the Small Business Administration.

Project No.: NIH 84-302

1. EDC ID No.: 2383

2. Entry Dates:

3. Status: In Process

4. Project Title: Stability of Selected Biomedical Research Domains Among Institutes Over Time

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD

7. Start/End Dates: 84-02, 86-01

8. Performer: In house

9. Agency Contact: Dr. Charles Lowe; NIH, Building 31, Room 2A20; (301)496-2500

10. Cost: FY 84-$33, FY 85- $46, FY 86-$11

11. Fund Source: Evaluation

12. Mechanism: In house

13. Project No.: NIH 84-302

14. Contract No.: NA

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Research and Data Development

19. Descriptors: Statistical Analysis Methods Feature, Statistical Data Feature, Trends and Forecasts, Information Systems, Research and Evaluation Methods Feature, Grant and Contract Management

20. Abstract: The project tracks biomedical research fronts through time using NIH grant activity and the article literature. Clusters of NIH grants are generated based on the co-occurance of CRISP terms. (Each grant is indexed by a set of 12-15 CRISP descriptors.) The grants in a cluster correspond to a biomedical research front. A pilot study of the grants active in 1982 from endocrinology and reproductive biology study sections generated clusters that were validated through interviews with intramural scientists active in these areas. All the new R01 grants have been clustered in each year from 1972 to 1984. Methods have been developed to link the clusters from year to year. The 1983 all-NIH R01 clusters have been validated in the same manner as the pilot study. Several longitudinal research fronts are undergoing indepth analysis involving interviewing scientists. Grant clusters will be linked to the article literature through the NLM/MESH and ISI citation data bases. The research fronts will be tracked in regard to NIH funding and Institute (BID) distribution overtime. The coverage will be national in scope.

1. EDC ID NO.: 2384 Project No.: NIH/DRG 84-301

2. Entry Dates: 3. Status: In process

4. Project Title: Development of a Program Evaluation Information System of Grant Applicants, Trainees, and Fellows

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 7/84 10/86

8. Performer: In house

9. Agency Contact: Dr. Doris Wallace; NIH, Westwood Building, Room 1A07; (301) 496-7264

10. Cost: FY 84 $3 FY 85 $20 FY 86 $17

11. Fund Source: Evaluation 12. Mechanism: In house

13. Project No.: NIH/DRG 84-301 14. Contract No.: NA

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Support

19. Descriptors: Information Systems, Management Information and Reporting, Research and Evaluation Planning and Administration.

20. Abstract:

A Program Evaluation Information System will be developed with data from the Grant Applicant and Trainee Fellow Files. These files enable a user to obtain data about NIH and ADAMHA applicants and awardees pertinent to evaluation studies such as his/her previous training support, type of degree, applications submitted, priority scores, education and research fields, etc. The records have been linked by an algorithm incorporating several items of information about the individual. Users with minimal computer expertise will be able to query the files to produce their own files and reports of relevant data. Future enhancements will include improving the retrieval process and linking records to current IMPAC data files.

Project No.: NIH/DRG 84-302

1. EDC ID No.: 2386

2. Entry Dates: 3. Status: In Process

4. Project Title: Comparison of Shortcomings in Clinical, Basic and Behavioral Research Grant Applications

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 84-02, 86-06

8. Performer: Contractor: W. Glen Moss, Ph.D., R.R.3, Box 1226, Front Royal, VA 22630; Inhouse staff

9. Agency Contact: Janet M. Cuca, NIH, Westwood Building, Room 455, (301)496-5352

10. Cost: FY 84 - $19

11. Fund Source: Evaluation 12. Mechanism: Contract, Inhouse

13. Project No.: NIH/DRG 84-302 14. Contract No.: 263-84-C-0107

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS - NIH- Biomedical Research (Entire Program Area)

18. Evaluation Type: Research and Data Development

19. Descriptors: Research and Evaluation Planning and Administration; Quality Assurance;

20. Abstract: This evaluation expands on and refines a previous project (published in Clinical Research 31:453-461, 1983) to examine the frequencies and types of shortcomings in research proposals submitted as NIH grant applications. The focus will be on differences among: (a) fundamental, laboratory, clinical, and behavioral projects; (b) highly-rated, poorly-rated, and disapproved applications, and (c) the fundamental, clinical, or mixed orientation of the review panel/study section reviewing the application. The "summary statements" (which report the review conclusions of the study section) for approximately 2,500 selected research proposals are being coded by a reader under contract; analysis and report writing will be done by inhouse staff. Data on the approval status and priority score of the application and on the training of the investigator submitting the application will be obtained from the NIH IMPAC system and used to examine patterns in the frequency and types of shortcomings. Results will be reported in an agency report and ultimately in a journal publication.

Project No.: NIH/DRS 84-301

1. EDC ID No:

2. Entry Dates:

3. Status: In process

4. Project Title: Evaluation of the Scientific Equipment Rental Program

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD

7. Start/End Dates: 85/11, 86/10

8. Performer:

9. Agency Contact: Howard Metz; NIH Building 13, Room 3W44; (301) 496-4656

10. Cost: FY 86-$95

11. Fund Source: Evaluation

12. Mechanism: Contract

13. Project No.: NIH/DRS 84-301

14. Contract No.: N01-RS-62103

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH - Scientific Equipment Rental Program

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Biomedical Research, Management Techniques, Benefits-Cost Analysis Feature, Consumer Evaluation Feature.

20. Abstract: During the past decade the Scientific Equipment Rental Program has evolved from a pool of surplus or donated equipment to an activity with $7 million in equipment and a dollar flow in excess of $1.5 million per year. The program runs on a no profit, no loss basis and has as the primary goal to accumulate and rent scientific equipment that has general utility in research work but is not sufficiently used by particular laboratories to warrant permanent possesion. The purpose of the evaluation effort is to provide a comprehensive and objective analysis of DRS's Scientific Equipment Rental Program. The evaluation will determine through questionnaires and interviews whether present and former customers of the service remain satisfied; review program objectives for comprehensiveness and consistency; identify and refine as necessary, evaluation criteria for each of the program objectives; examine program objectives to determine whether each is clear, measurable and realistic; identify service areas that should receive increased or decreased emphasis.

1. EDC ID No.: Project No.: NIH/DRS 84-303

2. Entry Dates: 3. Status: In-process

4. Project Title: Evaluation of the NIH Library Automated System

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 85-09, 86-05

8. Performer: King Research Inc., 6006 Executive Blvd., Rockville, MD 20852

9. Agency Contact: Carolyn Brown;
Building 10, Room 1L25G;
(301) 496-2447

10. Cost: FY 85-$59

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIH/DRS 84-303 14. Contract No.: N01-RS-52119

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Office of the Director-Library Services

18. Evaluation Type: Program Management or Efficiency, Program Performance Evaluation

19. Descriptors: Library Services, Information Processing, Productivity, Research and Evaluation Performance

20. Abstract: The NIH Library has installed an automated system designed to speed service delivery in circulation, interlibrary loan, cataloging, and information retrieval. This system will be evaluated for overall effectiveness and in comparison to previous manual methods. The contractor will use data previously collected and will collect data from specific operational categories affected by the system. The contractor will also observe and interview selected staff and library users. An assessment will be made of the effects of the system on the library user, of the cost/benefits of the online catalog, and of the advisability of changes in hardware/software.
include costs or other impact on agency resources. Reports will be submitted orally and in writing.

1. **EDC ID No.**: 2518 — **Project No.**: NIH/DRS 84-304

2. **Entry Dates**:

3. **Status**: In-Process

4. **Project Title**: Short-Term Evaluation of the Veterinary Resources Branch

5. **Report Title**: Phase I: Evaluability Assessment of Small Animal and Carnivore Program; Phase II: NYD

6. **Agency Sponsor**: PHS-NIH-OD

7. **Start/End Dates**: 84/10,85/11

8. **Performer**:

Primary
Aurora Associates, Inc.
1140 Connecticut Ave. N.W.
Washington, DC 20036

Subcontractor
James Bell and Associates
1700 North Moore Street
Arlington, VA 22209

9. **Agency Contact**:

Tom Ingalls; NIH
Bldg. 14G, Rm. 102;
(301) 496-3347

Cherie Nichols; NIH
Bldg. 12A, Rm. 4051
(301) 496-4501

10. **Cost**: FY 84-$51, FY 85-$84 ($17)

11. **Fund Source**: Evaluation

12. **Mechanism**: Contract

13. **Project No.**: NIH/DRS 84-304

14. **Contract No.**: 263-84-C-0356

15. **NTIS No.**: EDC Only

16. **ERIC No.**: NA

17. **Program(s) Evaluated**: Laboratory Animal Production and Holding

18. **Evaluation Type**: Program Performance Evaluation

19. **Descriptors**: Biomedical Research, Supportive Services, User Charges

20. **Abstract**: The study's objective is to assess the current status of Veterinary Resources Branch Services available to NIH intramural research programs to determine which activities could potentially be improved. The study will provide Division of Research Services management with information necessary for planning program changes and resource allocation. It will also identify areas of service that would benefit from a more comprehensive evaluation. Special emphasis will be placed on small animal and carnivore activities. The conduct of the study will involve the review of historical data on use of services and expenses for these activities and a direct survey of NIH intramural users to determine future requirements. The contractor will develop a model of program activities, objectives and performance measures, and then present alternative approaches along with full cost implications, expected benefits, and strategies for implementation. Reports will be presented verbally and in documented form.

Project No. NIH/NLM 84-301

1. EDC ID No.:

2. Entry Dates: 3. Status: In Process

4. Project Title: Evaluation of Medical Information Science (Medical Informatics)

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-OD 7. Start/End Dates: 85-01, 86-03

8. Performer: Association of American Medical Colleges, One Dupont Circle, N.W., Washington, D.C. 20036

9. Agency Contact: Dr. Elliot Siegel, NIH, Building 38, Room 2S-18 (301) 496-8834

10. Cost: FY 84 - $125; FY 85-0

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIH/NLM-84-301 14. Contract No.: N01-LM-4-3515

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research, Information Processing, Information Dissemination, Educational Technology, Information Systems, Medical Training

20. Abstract: The Association of American Medical Colleges (AAMC) is under contract to evaluate the status of medical information science in medical education and academic medical centers, and to make recommendations for appropriate future action. The evaluation effort is examining ways in which computers and information science technologies can improve medical education by de-emphasizing memorization and stressing information organization and problem solving as more appropriate methods of learning in a profession which requires independent life-long learning. Special attention is being given to the process of clinical decision-making as the development of databases and new knowledge in this field offers enormous potential for improving the efficiency and ultimately the cost of patient care applications. The use of new technologies, including information storage and retrieval, mathematical modeling, and database creation and maintenance can also support the biomedical research mission of academic medical centers. Finally, issues relating to manpower needs, training and incentives are also being considered.

Project No.: NIH 85-301

1. EDC ID No.: 2538

2. Entry Dates:

3. Status: In Process

4. Project Title: Evaluation of the Utility of a Database Management System for a Program Information System

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-OD

7. Start/End Dates: 85/1, 86/1

8. Performer: Staff

9. Agency Contact: Sheldon Fishman, NIH, Building 1, Room 228
(301) 496-4418

10. Cost: FY 85-$6, FY 86-$20

11. Fund Source: Evaluation

12. Mechanism: In-house

13. Project No.: NIH 85-301

14. Contract No.: NA

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts

18. Evaluation Type: Program Management

19. Descriptors: Information Systems, Federal Administration Grant and Contract Management, Management Information and Reporting

20. Abstract: A working group is evaluating the potential of a database management system to improve on current systems used to retrieve program information. Over many years, NIH has developed a sophisticated computer-based information system (IMPAC) on the extramural programs at NIH. This system is totally integrated into the tracking and administration of the extramural program. For example, IMPAC generates the postcards acknowledging receipt of an application and produces scoring sheets for Study Section members. Bureaus/Institutes/Divisions (BIDs) also make use of data in IMPAC for program management and evaluation. However, generally BIDs do not use IMPAC directly for program management. Usually a BID extracts data from IMPAC, feeds these data into a separate management information system and adds additional data (e.g. data from CRISP). This evaluation is examining whether the modern database management systems are likely to be useful to a BID in improving the performance of its management information system. For example, can a database management system improve on current methods to answer an urgent request for a report on current grants in a particular field of science. Generally, an Institute would search the CRISP system for grant identifiers, use those identifiers to locate data from the IMPAC system, and then format a report. To date, the working group have described their current program information systems and developed performance criteria a database management system must meet to be useful at NIH.

1. EDC ID No.:

Project No.: NIH 85-302

2. Entry Dates:

3. Status: In process

4. Project Title: Evaluation of Sources of Research Training of U.S. Professors of Medicine

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-OD

7. Start/End Dates: 85-07,86-09

8. Performer: Association of Professors of Medicine, 655 Fifteenth Street, NW, #425, Washington, DC 20005

9. Agency Contact: Dr. Charles R. Sherman, NIH, Building 1, Room 228, (301) 496-4418

10. Cost: FY 85-$72

11. Fund Source: Evaluation

12. Mechanism: Contract

13. Project No.: NIH 85-302

14. Contract No.: N01-OD-5-2103

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Training

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research, Research and Evaluation Performance

20. Abstract: This evaluation study will provide, for the first time extensive statistics describing the length, location, sources of support and other characteristics of research training of all faculty in U.S. medical schools. The portion of training provided through various NIH mechanisms will be highlighted. Principal investigators will be enumerated and compared with other researchers and with non-researchers. It is hoped that the descriptive data will display a pattern of training that leads to effective research participation and publication. The data derive from a two-wave survey conducted by the Association of Professors of Medicine and the faculty roster of the Association of American Medical Colleges.

Project No.: NIH/NHLBI 85-303

1. EDC ID No.:

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of the Clinical Investigator Award (CIA): Design of a Follow-up Evaluation

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH- NHLBI

7. Start/End Dates: 85-01, 86-12

8. Performer:

9. Agency Contact: Roth, Carl; NIH, Building 31, Room 5A11; (301) 496-3620

10. Cost: FY 86-$50

11. Fund Source: Program

12. Mechanism: Contract; In-house

13. Project No.: NIH/NHLBI-85-303

14. Contract No.:

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Scientific Manpower, Research and Evaluation Methods Feature

20. Abstract: Clinical Investigator Award (CIA) Programs have been widely adopted at the NIH as a means to attract young physicians into research careers. Since the first cohort of NHLBI awardees will complete their award terms in June 1985, it is timely to plan now for the follow-up evaluation to assure that necessary data can be collected. The NHLBI will rely primarily upon Institute and NIH staff to develop the plan, but will draw upon outside consultants as needed. As a first step, a panel of Institute and NIH staff will identify and agree upon appropriate program performance measures and comparison groups. It is expected that the agreed upon measures and comparisons will expand upon those included in the summer 1983 NHLBI study. The panel will then meet with outside consultants who are knowledgeable and experienced in bibliometric techniques and biomedical manpower issues to determine the feasibility of acquiring the data necessary for the planned measures and comparisons within a reasonable budget. Small scale data collection and analyses efforts will be attempted where issues of feasibility and economy of data collection arise.

Project No.: NIH/NICHD 85-304

1. EDC ID No.:
2. Entry Dates:
3. Status: In Process

4. Project Title: On-Line Planning and Evaluation Network (OPEN) Project [formerly called Design & Development of Prototype Program Information System to Facilitate NIH BID Planning & Evaluation Functions]

5. Final Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NICHD

7. Start/End Dates: 85/04, 86/09

8. Performer: Infodata Systems, Inc.
5205 Leesburg Pike
Falls Church, VA 22041

9. Agency Contact: Lynda C. Bennett
Building 31, Room 2A-10
(301) 496-1877

10. Cost: FY85-$36 ,FY86-$59 ,FY -$,FY -$,FY -$

11. Fund Source: Evaluation

12. Mechanism: In House Contract

13. Project No.: NIH/NICHD 85-304

14. Contract/Grant No.: 263-FD-529315

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Program Management

19. Descriptors: Information Systems

20. Abstract:

The Office of Planning and Evaluation (OPE) of the National Institute of Child Health and Human Development is nearing completion of a prototype information system which will provide descriptions of the Institute's research objectives and the activities undertaken to achieve those objectives. The prototype is being developed using off-the-shelf software which is easy to use and allows great flexibility in accessing the information in the system. The system will reside on the mainframe computer at NIH, allowing access to managers throughout the Institute. Following completion of the prototype, OPE will evaluate the efficiency of the system and its usefullness to various segments of the Institute.

1. EDC ID No. Project No.: NIH/NIDR 85-305

2 Entry Dates: 3. Status: In Process

4. Project Title: Evaluation of the NIDR Data Information Vocabularies

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIDR 7. Start/End Dates: 10/85, 9/86

8. Performer:

9. Agency Contact: Lynn, Dr. Kenneth C., Westwood Bldg, Rm 535, NIDR, NIH
(301) 496-7220

10. Cost: FY 85--$71

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIH/NIDR 85-305 14. Contract No: 263-85-C-0217

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: NIDR Data Information Vocabularies

18. Evaluation Type: Program Management

19. Descriptors: NIDR Information Vocabularies

20. Abstract: The two NIDR indexing vocabularies and the Computer Retrieval of Information for Scientific Projects (CRISP) vocabulary maintained by the Division of Research Grants will be evaluated to determine the need to maintain, refine, augment or combine the vocabularies in order to capture information needed by NIDR managers and policy makers. The results of the study will be disseminated through an agency report and technical manuals.

1. EDC ID No.   Project No.: NIH/NIDR 85-306

2 Entry Dates: 3. Status: In Process

4. Project Title: An Information System to Monitor the Performance of Thematic/Categorical Research Centers

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIDR   7. Start/End Dates: 9/85, 5/86

8. Performer:

9. Agency Contact: Brown, Dr. L. Jackson; Bldg 31, Rm 2C-36; NIDR, NIH
(301) 496-6705

10. Cost: FY 85-$9

11. Fund Source: Evaluation   12. Mechanism: In-house, Purchase Orders

13. Project No.: NIH/NIDR 85-306   14. Contract No: 263-MD-535117

15. NTIS No. NYD   16. ERIC No: NA

17. Program(s) Evaluated: NIDR Thematic and Categorical Centers

18. Evaluation Type: Program Impact

19. Descriptors: NIDR Thematic and Categorical Centers

20. Abstract: The NIDR has initiated a new program of thematic/categorical centers based on recommendations made through the Institute's planning and evaluation activities. An information system will be developed to monitor the research activities of centers of thematic/categorical research. The system will describe the types and amounts of research (both in dollars and numbers of projects) that thematic/categorical research centers undertake and relate this information to the goals and objectives of both the specific centers and of the Institute as a whole. The results of the study will be disseminated through agency reports.

Project No.: NIH 85-308

1. EDC ID No.: 2537

2. Entry Dates:

3. Status: In Process

4. Project Title: Statistical Algorithm to Link NLM MESH and NIH CRISP Vocabularies into a Single Dictionary

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-OD

7. Start/End Dates: 85-05, 86-09

8. Performer: In house staff and professional services contracts

9. Agency Contact: Dr. Charles Lowe; NIH, Building 31, Room 2A20; (301)496-2500

10. Cost: FY 85- $8 FY 86- $85

11. Fund Source: Evaluation

12. Mechanism: In house

13. Project No.: NIH 85-308

14. Contract No.: NA

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts

18. Evaluation Type: Research and Data Development

19. Descriptors: Literature Review Feature, Research and Evaluation Methods Feature, Trends and Forecasts, Library Services, Grant and Contract Management, Federal Role, Research and Evaluation Planning and Administration, Statistical Analyses Methods Feature, Information Processing, Information Systems

20. Abstract: This project will generate a correspondence dictionary between terms in the CRISP and MESH vocabularies. It will then be possible to take any funded NIH grant, extract its CRISP terms, find the corresponding MESH terms with the dictionary and locate the article literature relevant to the grant through the MESH system. The dictionary will allow both the identification of the literature produced by the grant and also topic relevant literature not produced by the grant. Moreover, once a MESH profile is established for a grant using the dictionary, the topic relevant literature can be traced through time. Pre-grant and post-grant activity in the area can then be assessed.

The method uses the MESH data from 1982-1983 which contains NSF acknowledgements. The CRISP terms will be accessed for the acknowledged NIH grants. Statistical associations will be built across the entire MESH file between MESH terms and CRISP terms associated through grant acknowledgements. These statistical associations will be used in an ordinal rank order algorithm to generate the dictionary.

1. **EDC ID No.**: 2534 **Project No.**: NIH 85-311

2. **Entry Dates**: 3. **Status**: In process

4. **Project Title**: Survey of Academic Biomedical Research Facilities: Status and Needs

5. **Report Title**: NYD

6. **Agency Sponsor**: PHS-NIH-OD 7. **Start/End Dates**: 84/11, 86/09

8. **Performer**: ABT Associates, Inc., 55 Wheeler Street,
Cambridge, Massachusetts 02138

9. **Agency Contact**: Dr. Helen Hofer Gee, NIH, Building 1, Room 228
(301) 496-4418

10. **Cost**: FY 85- $159, FY 86-$134

11. **Fund Source**: Evaluation 12. **Mechanism**: Contract

13. **Project No.**: NIH 85-311 14. **Contract No.**: NO1-OD-5-2100

15. **NTIS No.**: NYD 16. **ERIC No.**: NA

17. **Program(s) Evaluated**: PHS-NIH-Biomedical Research--Activity--Construction Grants

18. **Evaluation Type**: Research and Data Development

19. **Descriptors**: Biomedical Research, Research and Evaluation Planning and Administration, Facilities

20. **Abstract**: A survey of the status of and needs for construction renovation of biomedical research facilities is proposed by NIH. Draft survey instruments intended for universities and independent hospitals and research institutes have been developed. ABT Associates is completing the design of the instruments and conducting appropriate pretest studies at nine academic and nine independent research hospitals or laboratories. In addition to describing the age and condition of all relevant research space, respondents will report on construction completed during the past five years and planned for the next five years. Other urgent research facilities needs will also be described. The information obtained from the survey will respond to a request from both the House and Senate appropriations committees who want reports on facilities needs from NIH. In addition, NIH will utilize the information to assess the need for NIH involvement in developing and maintaining physical facilities for biomedical research.

4

NATIONAL CANCER INSTITUTE

Dr. Vincent T. DeVita, Jr., Director

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National Cancer Institute: Proposed Budget

		$ in Thousands		
		FY 85	FY 86	FY 87
NCI 82-303	Cancer Therapy Evaluation Program (CTEP) Information System	(600)	(228)	---
NCI 83-301	Integrated Evaluation of Community Cancer Care Programs	---	---	---
NCI 83-304	An Assessment of the Factors Affecting Critical Cancer Research Findings	(100)	---	---
NCI 83-305	Evaluation of NCI Mass Media Program Television Public Service Announcements	---	---	---
NCI 84-401	Evaluation of NCI's Cancer Communications Program	(100)	(281)	(281)
NCI 84-402	Development of the Cancer Control Tracking System	---	(250)	(250)
NCI 84-403/ 405	Evaluation of the International Cancer Research Data Bank	(34)	(125)	(22)
NCI 85-401/ 402	PDQ Users Group and Vendors Evaluation	---	(237)	(230)
	Total FY 86 NCI Evaluation Fund Request		(1,121)	

Note: ( ) non set-aside funds

1. NIH Evaluation Project Identifier: NCI 83-304

2. Project Title and Capsule Description:

   a. Title: An Assessment of the Factors Affecting Critical Cancer Research Findings

   b. Capsule Description: Frequently, statements are made concerning the relationship between administrative aspects of research, i.e., mechanism of funding (contracts, grants) or location of the performer (university, Federal agency, centers, private sector); and the scientific aspects, i.e., quality of the results, impact on the field or discipline. NCI proposes an evaluation project which will attempt to determine if the relationship between the administrative and scientific aspects of support and conduct of research is significant.

3. Agency Proposing: NIH - NCI

4. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)
83	200	---
84	275 (71)	---
85	(100)	---

Note: ( ) non set-aside funds.

5. Program(s)Evaluated: PHS-NIH-Biomedical Research (Entire Program)
   PHS-NIH-Biomedical Research-Activity-Intramural Research
   PHS-NIH-Biomedical Research-Activity-Grants and Contracts
   PHS-NIH-Biomedical Research-Institute Specific-Cancer

6. Purpose: To determine if the relationship between the administrative aspects of research (i.e., mechanisms of funding, location of performance) and the scientific aspects (i.e., quality of results, impact on the field) is significant.

7. Related Work: The NIH evaluation report entitled "An Analysis of Research Publications Supported by NIH" (1980) will provide some useful inputs to the proposed study, and other previous studies utilizing citation indexing and content analysis techniques will be useful also. But, to our knowledge, a study has not been done which specifically addresses the relationship of scientific and administrative factors, and the significance of their link to a given number of critical findings in cancer research.

8. Type and Approach Methodology:

   a. Type: Assessment of program policies to determine their impact on the activities of authorized programs.

   b. Approach/Methodology: It is proposed that a panel of scientists compile a list of scientific findings (nominally 10 to 15) that occurred during the past 10 years that have had the most significant impact on cancer research. Citation indexing and other bibliometric techniques can be used to assess the impact of these findings on cancer research. Content analysis (including the review of the original grant application or contract proposal) will be useful in determining if the research leading to the finding was initially described. A variety of statistical techniques may be valuable in determining the significance of the link between administrative factors (i.e., funding mechanisms and location of performance) and the quality of the scientific findings as determined by their impact on cancer research.

9. Project Origin and Intended Major Users:

   a. Project Origin: This general subject has been discussed at numerous NCI staff meetings over the years, and most recently at one of NCI's senior staff planning and budget formulation meetings. A more specific discussion was continued at one of the regularly scheduled meetings of the Director, NCI, and his immediate staff. Based on this discussion, it was decided that a study attempting to evaluate the significance of the linkage between administration and scientific factors would be appropriate for the 1% set-aside funds.

   b. Intended Major Users: This study is intended to provide some new information and insights on a frequently discussed subject. As such it should be of interest to all persons concerned with the processes of research support and with the analysis and evaluation of research results.

10. Application of Findings: The study results are intended to be used as reference material and to provide some new information concerning the relationship between administrative and scientific factors and research performance. It is not the specific intention of the study to provide a basis for directly influencing policies associated with the review and selection of research or the mechanisms of funding.

11. Project Description Submission and Approval Dates:

Date first submitted	April 1982
Date revision submitted	
Date approved	

12. Execution: The project will be performed by contract administered by NCI. The project will require the preparation of a completely unbiased report. Personnel having the appropriate skills and knowledge required for this project are not presently employed by the NCI, and if they were hired, most likely could not be fully utilized by the NCI after completion of this project. With these considerations in mind, the contract mechanism is the instrument of choice.

Project Description Approved	August 1982
RFP Issues	January 1983
Contract Signed	September 1983
Preliminary Findings Available	September 1985
Final Report Available	March 1986

13. Project Monitor/Contract:

Mr. Louis M. Carrese
Associate Director for Program Planning and Analysis
Office of the Director, NCI
Bldg. 31, Room 10A52
NIH, Bethesda, Maryland 20892
(301) 496-6445

14. Coordination: The NCI Director's immediate staff and the staff of the office of Program Planning and Analysis have reviewed the project. General oversight will be performed by the NCI Executive Committee.

15. Information Collection Burden: To be determined.

1. EDC ID No: 2090 Project No: NCI 80-304

2. Entry Dates: 3. Status: Complete

4. Project Title: Evaluation of Cancer Communications Network (Phase I)

5. Report Title: Evaluation of Cancer Communications Network (Phase I)

6. Agency Sponsor: PHS-NIH-NCI 7. Start/End Dates: 82-04, 84-10

8. Performer: NCI Staff and Evaluation Consultant

9. Agency Contact: Judith Stein, Blair Building, Room 414, (301) 427-8656

10. Cost: FY 83 - $8 ($60)
FY 84 - $10

11. Fund Source: Evaluation 12. Mechanism: In house staff and Professional Service Contra

13. Project Number: NCI 80-304 14. Contract Number: N/A

15. NTIS No.: NYD 16. ERIC No.: N/A

17. Programs Evaluated: PHS-NIH-Biomedical Research - Activity - Program Management and Direction

18. Evaluation Type: Program Management of Efficiency

19. Descriptors: Cancer, Outreach and Referral, Information Dissemination

20. Abstract: The purpose of the project is to provide a program evaluation of the Cancer Communications Network (CCN), consisting of 17 regional programs. Each office operates a telephone information system known as the Cancer Information Service or CIS. The CIS staff responds to inquiries from the lay public, cancer patients and their families, and health professionals. The NCI recognized the need for setting uniform reporting, performance and quality standards for the CIS program. This project involved the development, pilot testing and implementation of a common data collection instrument, a survey of CIS users, and a method for determining quality of response to CIS inquiries. Developmental work was done by NCI staff assisted by an Evaluation Task Force. Evaluation funds were used to obtain the services of a consultant to assist in the implementation of the CIS survey of users and the quality control system consisting of test calls placed to regional CIS offices.

Project No.: NCI 82-303

1. EDC ID No.: 2141

2. Entry Dates: 3. Status: In-process

4. Project Title: Cancer Therapy Evaluation Program (CTEP) Information System

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NCI 7. Start/End Dates: 82-08, 86-09

8. Performer: Information Management Services, Inc.
6110 Executive Boulevard, Suite 310
Rockville, Maryland 20852

9. Agency Contact: Donald Poppke, Landow Building, Room 4A22, 496-1181

10. Cost: FY 82 - ($272); FY 83 - $270 ($218); FY 84 - ($648); FY 85 - ($600); FY 86 ($228)

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NCI 82-303 14. Contract No.: NO1-CM-27510

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH - Biomedical Research-Institute Specific - Cancer

18. Evaluation Type: Research and Data Development

19. Descriptors: Cancer, Information Processing, Medical Practice

20. Abstract:

The prime purpose of the CTEP-IS is the development of a protocol information system. A modular approach has been used for this development; the three modules of information are "Administrative", "Scientific", and "Results". In conjunction with this modular approach, two major tasks have been undertaken. One has been the initiation and completion of a Phase II single agent protocol subsystem involving all three modules of information. This subsystem is now complete and has been incorporated into the main CTEP-IS. The second, and still ongoing, task is the development of the main CTEP-IS, which has been developed in two phases. The "Administrative Tracking System" is now complete and incorporates the "Administrative" information module and some of the "Scientific" information. The second phase, which is now being implemented, is the development of a linkage with the NCI Protocol Data Query (PDQ) system.

The Drug Distribution and Protocol Monitoring System (DDPMS) is a drug oriented data base which is maintained and operated by VSE Corporation, subcontractor to Information Management Services, Inc. The system is an automated and manual support procedure used to verify the accuracy of clinical drug requests made by investigators. It also maintains complete drug distribution histories by investigator, protocol, drug and dose form. Currently there are 105 investigational drugs used by 5,000 investigators on protocols. Approximately 1,500 individual drug requests (line items) are made by investigators each month. It is the Food and Drug Administration requirement that IND sponsors only provide investigational drugs to registered investigators for use on approved studies. The DDPMS plays a major role in assuring that these requirements are met.

1. EDC ID No.: 2130 Project No.: NCI 83-301

2. Entry Dates: 3. Status: In Process

4. Project Title: Integrated Evaluation of Community Cancer Care Programs

5. Report Title: Not Yet Determined

6. Agency Sponsor: PHS-NIH-NCI 7. Start/End Dates: 83-09, 86-08

8. Performer: Fred Hutchinson Cancer Research Center
Statistical Analysis and Quality Control Center
Seattle, Washington 98104

9. Agency Contact: Leslie G. Ford, M.D.
Blair, Room 7A01 427-8708

10. Cost: FY83 - $200 ($618)
FY84 - $1,096 ($1,874)

11. Fund Source: Evaluation and Program 12. Mechanism: Contract

13. Project No.: NCI 83-301 14. Contract No.: N01-CN-35009

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS - NIH - Biomedical Research -
Institute Specific-Cancer

18. Evaluation Type: Program Management or Efficiency

19. Descriptors: Cancer, Community Cancer Care, Planning, Technology Transfer

20. Abstract: The purpose of this project is to carry out an integrated evaluation of the Cooperative Group Outreach Program, the Community Hospital Oncology Program and the Community Clinical Oncology Program to determine the extent to which the programs independently and through their interactions lead to changes in the patterns of cancer care in the communities and to the introduction of new technology into patient care management. Six Cooperative Group Outreach Programs have been funded since 1976. Seventeen Community Hospital Oncology Programs were funded in July 1982 for implementation (RFP-NCI-CN-25009-49). Sixty-two Community Clinical Oncology Programs were implemented in September 1983 for three years.

While each of the programs differs slightly in emphasis and essential elements, they all have the same primary goal - to establish a mechanism to facilitate the transfer of new patient care technology to the community and thereby to provide the highest quality cancer management to patients in the community setting. The major mechanism is community participation in clinical research.

The initial phase of the project involved identifying specific research questions and the detailed design to employ to obtain their answers. Four research questions were developed:

- Is there an increase in participation in clinical research protocols as a result of the programs?
- Are there changes in patterns of cancer patient management as a result of the programs?
- Are there changes in the health care systems where programs exist?
- What are the characteristics of a successful community cancer program?

The detailed design of the evaluation uses a multi-tiered approach which includes analyzing descriptive data; examining patterns of cancer care for breast, oat-cell lung, and colorectal patients before and during the programs; and conducting indepth organizational studies and a physician survey early and late in the programs. Control programs (CCOP applicants that were approved but not funded) have been included in each tier to strengthen the overall design and analysis of the study.

The evaluation, scheduled for completion in three years, will provide critical information for the design of future community cancer programs.

1. EDC ID No. 2140 Project No.: NCI 83-305

2. Entry Dates: 3. Status: In process

4. Project Title: Evaluation of the NCI Mass Media Program: Television Public Service Announcements

5. Report Title: NYD

6. Agency Sponsoring: PHS-NIH-NCI 7. Start/End Dates: 84-07, 86-02

8. Performer: Nancy Low and Associates (contractor)

9. Agency Contact: Rose Mary Romano, Bldg. 31, Rm. 4B41, 496-6792

10. Cost: FY 83 - $35

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NCl 83-305 14. Contract No.: NCI-CO-33851

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS - NIH - Biomedical Research - Institute Specific - Cancer

18. Evaluation Type: Program Management or Efficiency

19. Descriptors: Cancer, Educational Technology, Information Dissemination, Broadcast Technology

20. Abstract: This project will evaluate NCI mass media program, specifically its television public service announcements (PSA) and will examine media penetration (share of the public service airtime) and placement (time of day messages are shown). For a three-month period broadcast airtime will be monitored to determine the content, source, number of plays and time of day of all health public service announcements. An analysis will compare the NCI PSA airtime to that allotted for all health PSAs. This will enable the Office of Cancer Communications to measure the relative success of its PSA in relation to all other health PSAs.

1. EDC ID No.: Project No.: NCI 84-401

2. Entry Dates: 3. Status: In process

4. Project Title: Communications Program Evaluation Support Contract

5. Report Title:

6. Agency Sponsor: PHS/NIH/NCI 7. Start/End Dates: 84-04, 87-03

8. Performer: D.K. Shiflett & Associates, Ltd., Westgate Research Park, Suite 216, 7710 Old Springhouse Road, McLean, VA 22102.

9. Agency Contact: Barbara Blumberg, Building 31, 4B-39, (301) 496-6792

10. Cost: FY 85-($100); FY 86-($281); FY 87-($281)

11. Fund Source: Program 12. Mechanism: Contract

13. Project No.: NCI 84-401 14. Contract No.: N01-CO-54059

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research - Institute Specific - Cancer

18. Evaluation Type: Research and Data Development

19. Descriptors: Cancer, Communications

20. Abstract: This contract is designed to plan and implement evaluation of the Office of Cancer Communications' programs and products, including the national Cancer Education Program in particular. Techniques will include survey research, media research studies, and formative process as well as summative evaluation. A master evaluation plan will be written in the first six months of the project and completed at 18 months with NCI staff and subcontractors (CDP and Low & Associates) participating.

The results of the proposed evaluation project will be used by the Office of Cancer Communications for guiding overall policy and program management; making appropriate changes in present programs and materials; planning for future efforts; providing evidence to support continuation of office activities; reporting on OCC activities to Congress and other interested parties; promoting broader replication and dissemination of successful projects and approaches; and helping other organizations within the National Cancer Program to improve their communication efforts.

Project No.: NCI 84-402

1. **EDC ID No.:**

2. **Entry Dates:** 3. **Status:** In process (awaiting technical review)

4. **Project Title:** Development of the Cancer Control Tracking System

5. **Report Title:** NYD

6. **Agency Sponsor:** PHS-NIH-NCI 7. **Start/End Dates:** 85-09, 90-08

8. **Performer:** (Awaiting technical review of proposals)

9. **Agency Contact:** Robert Parke, Blair Bldg., Room 4A01, (301) 427-8735

10. **Cost:** FY 86-($250); FY 87-($250); FY 88-($250); FY 88-($250); FY 90-($250)

11. **Fund Source:** Cancer Control 12. **Mechanism:** Contract

13. **Project No.:** NCI 84-402 14. **Contract No.:** NYD

15. **NTIS No.:** NYD 16. **ERIC No.:** NA

17. **Program(s) Evaluated:** PHS-NIH-Biomedical Research-Institute Specific Cancer

18. **Evaluation Type:** Research and Data Development

19. **Descriptors:** Cancer/Preventive Health Care/Public Health Services/Facilities/Health Care Delivery Systems

20. **Abstract:** This contract provides for the development of a database and reports on cancer control activities and programs in the Federal and non-Federal Government, voluntary and private sectors. The contractors will identify and appraise existing data on programs and activities that may be relevant to attainment of the NCI's year 2000 goals, propose plans for development of the database, compile and collect data as directed, and prepare reports.

Project No: NCI 84-403/405

1. **EDC ID No.:**

2. **Entry Dates:** 3. **Status:** In Process

4. **Project Title:** Evaluation of the International Cancer Research Data Bank

5. **Report Title:** NYD

6. **Agency Sponser:** PHS-NIH-NCI 7. **Start/End Dates:** 85-08, 87-03

8. **Performer:** National Cancer Institute, Office of International Affairs,
International Cancer Information Center

9. **Agency Contact:** Linda W. Blankenbaker, Building 82, Room 119, (301) 496-4907 or 9096

10. **Cost:** FY 85-($34); FY 86-($125); FY 87-($22)

11. **Fund Source:** Operating Budget 12. **Mechanism:** Contract

13. **Project No.:** NCI 84-403/405 14. **Contract No.:** N01-C054051

15. **NTIS No.:** NYD 16. **ERIC No.:** N/A

17. **Program(s) Evaluated:** PHS-NIH - Biomedical Research-Institute Specific - Cancer

18. **Evaluation Type:** Research and Data Development

19. **Descriptors:** Cancer, International Cancer Information Center, Information Dissemination, Survey or Questionnaire Feature

20. **Abstract:** This evaluation of International Cancer Information Products and Services is concerned with users and potential users. It will examine what information they need, how they prefer to obtain it, and what use they make of it. The evaluation will also consider International Cancer Information Center products and services as related to other cancer information, its producers, distributors, and users. The evaluation is expected to identify changes which will enable the International Cancer Information Center to provide subscribers and users the information they need and to increase awareness among potential users of International Cancer Information Center information products and services.

Data will be gathered and analyzed through several mechanisms. The major activities will be a series of mail surveys conducted with the broad cancer research community, libraries providing International Cancer Information Center services, and individual product users. Data from the surveys will be used to determine levels of awareness and use. The combined subscriber/user file will be analyzed to distinguish between and relate institutional and individual subscribers and users. Surveys will yield demographic data, knowledge about use of primary and secondary information sources and preferences, evaluative data, potential changes, and purposes of use of International Cancer Information Center products and services. The target respondents are a broad audience of cancer researchers, librarians, and specific product users. Survey yield reports will be submitted to the International Cancer Information Center along with an overall evaluation report describing the combined results and their implications. No official formal publication is intended.

1. **EDC ID No.:** **Project No.:** NCI 85-401/402
2. **Entry Dates:** 3. **Status:** In Process
4. **Project Title:** PDQ User Groups and Vendors Evaluation
5. **Report Title:** NYD
6. **Agency Sponsor:** PHS-NIH-NCI 7. **Start/End Dates:** 85-10, 87-09
8. **Performer:** NYD
9. **Agency Contact:** Edward Maibach, M.P.H.
Blair 413
427-8656
10. **Cost:** FY 86-($237); FY 87-($230)
11. **Fund Source:** S & E 12. **Mechanism:** Contract
13. **Project No.:** NCI 85-401/402 14. **Contract No.:** NYD
15. **NTIS No.:** NYD 16. **ERIC No.:** NA
17. **Program(s) Evaluated:** PHS-NIH-Biomedical Research-Institute Specific-Cancer
18. **Evaluation Type:** Program Performance Evaluation
19. **Descriptors:** Cancer, Information Dissemination, Questionnaire Feature, Information Systems, Educational Technology, Research Evaluation Planning and Admin.
20. **Abstract:** PDQ is an on-line cancer information system designed by the NCI to improve the Nation's cancer care system. PDQ makes the latest information on cancer treatment, research protocols and referral sources readily available to physicians, all geographically indexed by region to facilitate its effective application. Widespread adoption of PDQ by members of the medical community may positively affect the stage at which cancers are identified, proper diagnosis, optimal treatment, and the rate of patient accrual into clinical protocols. The importance of these factors indicates the need for a thorough evaluation. This evaluation will provide feedback with which to modify and improve PDQ.

Physicians and their information intermediaries are the focus of this evaluation. Information will be collected on the technical performance of the system, adopters and non-adopters of the system, system use, and indicators of system impact. Data will be gathered with a variety of techniques, including surveys, automated usage data, user panels, and focus groups.

5

NATIONAL EYE INSTITUTE

Dr. Carl Kupfer, Director

Contents

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National Eye Institute: Proposed Budget

		$ in Thousands		
		FY 85	FY 86	FY 87
NEI 82-401	Design of a System for Evaluating the Implementation of the NEI 1983-1987 Program Plan	--	($50)	--
NEI 83-301	Evaluation of the NEI Small Grants Program	--	—	—
NEI 86-401	Midcourse Evaluation of Third NEI Plan	--	($10)	--
	Total FY 86 NEI Evaluation Fund Request		($60)	

NOTE:

( ) Non Set-Aside Funds

New Project Not Reviewed by NIH Technical Review Committee

NEI 86-401--Midcourse Evaluation of Third NEI Plan

This evaluation project, which will include publication of a 100-page report, is examining the current level and distribution of effort in all the scientific research areas addressed by Vision Research--A National Plan: 1983-1987, the National Advisory Eye Council's most recent planning and evaluation document, (NEI 80-306: Third Formal NEI Program Evaluation and Planning Process). It will recognize and encourage activity in important new areas which have developed since the Plan was prepared or which are just now emerging. And it will identify recommendations that may not have been sufficiently specific or those that may have been premature or were too narrow in focus and might benefit from consolidation with other recommendations.

Accordingly, the Council has charged the Panels that have been convened for the midcourse evaluation with the following tasks:

A. Review the recommendations in each subprogram or area of the relevant panel report in the current Plan.

B. Review updated Resource Tables that the NEI staff will provide which show in detail the actual NEI funding experience in FY 1982-1984.

C. Ask the following questions:

(1) Do the Program Base and Program Development Priorities identified in the Plan adequately describe the full scope of current research in this field? Is there a compelling need now to revise, add, or eliminate certain categories?

(2) Is there an appropriate balance of effort among and within subprograms as recommended in the Plan in terms of the stated program goals and objectives?

(3) Are the original project and budgetary recommendations for FY 1983, as shown in the Plan's Resource Tables, still appropriate for FY 1986-1987?

D. Update the Program Base and Program Development Priorities, giving a brief rationale for any changes.

E. Identify, along with a few paragraphs of justification (according to a standard format that will be provided):

(1) Any major areas of the current Plan that should be revised.

(2) Any "hot" new areas of research that should be considered for future development and which should be discussed in depth in the next National Plan.

Although the current National Plan is the third in a series, we have not until recently had a practical means for assessing in detail and on a continuing basis the implementation of the dozens of recommendations made by the panels of experts that the Council and the NEI convened to examine research needs and opportunities and to identify program priorities. To this end, the NEI has established a computerized system for tracking grant applications wherein every grant application, whether funded or not, is coded according to its relevance to one of the Plan's recommendations. This system will be especially useful to the program-oriented panels during their assessment of the appropriateness of the current distribution of grants, particularly in view of the rapid pace of advancement in many fields of vision science which affords today's investigators opportunities that were not available when the current Plan was drafted during the years 1981-83. Such an assessment made midway in the current planning cycle will indicate any need for fine tuning the current plan, as well as provide an important basis for the preparation of the 1987-1992 Plan, which will get underway near the end of FY 1985.

The report produced in conjunction with this Midcourse Evaluation will be used by the National Advisory Eye Council and the staff of the National Eye Institute to determine long-range and day-to-day management decisions; by ophthalmic and optometric clinicians and others in the vision research community as a guide to the most important needs and opportunities in the field; and by organizations, foundations, and all those interested in recent problems and challenges in ophthalmology, optometry, and vision science, including current activities and plans for continued success in the prevention, treatment, and control of blinding eye diseases.

The audience for this report will be vision scientists, ophthalmologists, optometrists, and all those clinicians, investigators, and scientists interested in these fields; those who participated in the development of the current NEI plans; those who will help develop the next five-year plan; all National Eye Institute grantees; all university departments of ophthalmology; all schools of optometry; appropriate government offices; and all those who request it.

Announcements of the report's availability will be published in appropriate journals. Copies of the report will be distributed at annual meetings and workshops conducted by organizations fostering or supporting research in vision science and related fields. And the report will be mailed to medical school libraries, the membership of associations and foundations related to vision research, and to all those who request it.

The in-house and printing and distribution costs of this project are expected to total $10,000. The report will be available in the autumn of 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

Project No.: NEI 82-401

1. EDC ID No.: 2539

2. Entry Dates:

3. Status: In Process

4. Project Title: Design of a System for Evaluating the Implementation of the NEI 1983-1987 Program Plan

5. Report Title: N/A

6. Agency Sponsor: PHS-NIH-NEI

7. Start/End Dates: 84-10, 85-9

8. Performer: NEI staff with the National Advisory Eye Council

9. Agency Contact: Julian M. Morris
Associate Director for Planning, Analysis and Evaluation
National Eye Institute
National Institutes of Health
Building 31, Room 6A25
Bethesda, Maryland 20205
(301) 496-4308

10. Cost: FY 86-($50)

11. Fund Source: Evaluation

12. Mechanism: In-house

13. Project No.: NEI 82-401

14. Contract No: N/A

15. NTIS No.: NYD

16. ERIC No.: N/A

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Management
PHS-NIH-Biomedical Research-Institute Specific-Eye

18. Evaluation Type: Program Impact, Program Performance Evaluation

19. Descriptors: Planning, Research and Evaluation Planning and Administration, Management Techniques, Needs and Needs Assessment

20. Abstract: This project is evaluating the implementation of the new national plan for vision research. Fundamental to any assessment of the effectiveness of this national research plan, which is aimed at directing NEI resources toward high priority areas of vision research, is the development of a system that shows not only pertinent information about potention grantees and what correspondence there is between the subject matter of their grant applications and the program priorities established by the new plan, but also how well such applications fare in the review and funding process and what relationship there may be between submission of applications in priority areas and the funding of these proposals. It will be useful as well for NEI management to have analytical data on applications and funded grants for research in areas

not specifically indentifed as having high priority. This project is also tracking and evaluating whether the plan's recommendations are actually achieved by those research projects that are funded. This will be accomplished by analyses of progress reports, published papers, literature citations, and bibliometrics.

In addition to the Council and NEI program managers, the tracking system should provide data that can be made available to a wider audience, in particular, the scientific community and NIH and HHS officials. Evaluating the implementation of the NEI plan will carry forth the goals and objectives of the plan and demonstrate the credibility of that plan and the NEI's and its Council's commitment to fulfilling and updating it.

The data and analyses resulting from this system will be used as a basis for program relevance judgments by the Council and staff, periodic updating of the NEI's national plan, and for future development of new comprehensive five-year and other program evaluations and plans. These data and analyses will be examined by senior members of the NEI staff and by the Council to determine not only what correspondence there is between grant applications and identified program priorities and how well such applications fare in the review and funding process but also data concerning the potential investigators, for example, their ages, disciplines, history of experience with NEI-NIH grants and prior participation on NEI committees, and the comparison of the investigator's fields of interest prior and subsequent to the publication of the national plan. It will also be useful to the NEI staff and Council to note the applications received in areas not identified as high priority by the plan and, conversely, the areas seemed to be high priority but for which few, if any, applications have been received. Also, the use of progress reports, citation analysis, and bibliometric studies will help in judging the outcome of NEI-supported research projects. After two years of such study, sufficient data will have been gathered upon which preparations for an updated national plan may be based.

Project No.: NEI 83-301

1. EDC ID No.: 2367

2. Entry Dates: 3. Status: In Process

4. Project Title: Evaluation of the NEI Small Grants Program

5. Report Title: N/A

6. Agency Sponsor: PHS-NIH-NEI 7. Start/End Dates: 82-11, 85-10

8. Performer: NEI Staff

9. Agency Contact: Ronald Geller, Ph.D.
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10. Cost: FY 83-$2

11. Fund Source: Evaluation 12. Mechanism: In-house

13. Project No.: NEI 83-301 14. Contract No.: N/A

15. NTIS No.: NYD 16. ERIC No.: N/A

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Management
PHS-NIH-Biomedical Research-Institute Specific Eye

18. Evaluation Type: Program Impact, Program Performance Evaluation

19. Descriptors: Management Techniques, Research and Evaluation Performance

20. Abstract: This project is evaluating the National Eye Institute's Small Grants Program to determine whether it is achieving the goals for which it was designed: to support pilot projects, testing of new techniques, and feasibility studies of important, innovative, and high risk research--all of which would provide a basis for more extended research. The target population of the Small Grant Program includes: clinicians with limited research experience, recently trained or less experienced basic scientists, investigators whose research careers have been interrupted and are to be resumed, investigators changing fields of research, investigators at minority institutions or located in a largely nonresearch environment, and established investigators needing quick support for a pilot project.

The Small Grants Program was initiated on an experimental basis on October 1, 1981, for a period of two years to allow the NEI staff sufficient time for its evaluation before deciding whether it should be continued. As of May, 1984, a total of 447 Small Grant Applications have been reviewed; the NEI has awarded over 110 small grants for approximately $2.2 million in total costs. In addition to the National Eye Institute, several other Institutes have initiated or are considering Small Grants Programs.

The Small Grants Programs that now exist or are proposed by various Institutes have many similarities, including the fact that they consist of one-year nonrenewable grants for a maximum of $15,000 in direct costs. Most or all of the Small Grants Programs utilize methods for receipt and review of applications that shorten the time lapse between the receipt of an application and when an award is made. However, these programs differ in several review, programmatic, and administrative characteristics, thus allowing each to meet the research needs of its own Institute.

In view of these differences, it is important to evaluate all Small Grant Programs separately to determine what factors are most effective for each program. Conversely, it is clearly useful to coordinate and compare these evaluations. Such coordinating efforts have already begun in the form of discussions between NEI personnel and those who administer the Small Grants Programs of the National Institute on Aging and the National Institute for Dental Research. A copy of the NEI evaluation plan has been made available to evaluation personnel in the National Institute on Aging and to program personnel in the Division of Research Resources. It is expected that such inter-institute discussions and coordination in evaluating Small Grants Programs will continue and expand.

The two most important goals of this evaluation are to identify factors that should be considered in the review and administration of small grants and to assess the impact of the NEI Small Grants Program on vision research. Specifically, the evaluation seeks to examine the patterns of both successful and unsuccessful applicants to the program.

Objective data analysis will be done in house by a combination of in-house effort and contract. More subjective portions, as well as bibliometric analysis, are to be performed by contract. Results of this evaluation will be considered in determining whether the program should be continued. A key issue is to identify the best use for available research dollars, and it is therefore essential to determine how well the program meets existing research needs. Because several other institutes either already have estalished a small grants program or are considering doing so, the procedures and information obtained through this study may be helpful to managers and policy makers in other institutes.

6

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Dr. Claude Lenfant, Director

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NHLBI 84-406	Evaluation of the Impact of the Coronary Primary Prevention Trial (CPPT) on Public Attitudes, Knowledge, and Behavior Regarding Serum Cholesterol and Other Risk Factors for Coronary Heart Disease (CHD)	(84)	--	--
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National Heart, Lung, and Blood Institute:
Proposed Budget - Continued

		$ in Thousands FY 85	 FY 86	 FY 87
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NHLBI 85-404	Analysis of Antihypertensive Drug Prescriptions	(1)	--	--
NHLBI 85-405	High Blood Pressure: 1986 Survey of Physicians' Knowledge, Attitudes, and Reported Behavior	(74)	(251)	--
NHLBI 86-401	Coronary Heart Disease Risk Factors in Children: Current Physician Attitudes, Knowledge, and Practice	--	(50)	(150)
NHLBI 86-402	Knowledge, Attitudes, and Behavior of Nurses and Dietitians Regarding Cardiovascular Risk Factors	--	(75)	(200)
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NHLBI 86-405	Evaluation of Pulmonary Faculty Development Award	--	(30)	--
	Total FY 86 NHLBI Evaluation Fund Request		(788)	

Note: ( ) non set-aside funds

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NHLBI 86-401

2. Project Title and Capsule Description:

   a. Title: Coronary Heart Disease Risk Factors in Children: Current Physician Attitudes, Knowledge, and Practice

   b. Capsule Description: A sample of physicians with practices involving primary care for children will be surveyed to determine their attitudes, knowledge, and medical practice behaviors related to the prevention of heart disease in the young.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	($50)	-	($50)
87	($150)	-	($150)
88	($100)	-	($100)

Cost Justification: The cost estimate is based upon the cost of two recently performed physician surveys designed to assess the impact of the NHLBI-sponsored Coronary Primary Prevention Trial.

4. Project Monitor/Contact:

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5. Coordination: The project was reviewed and approved by the Preventive Cardiology Working Group of the NHLBI Clinical Applications and Prevention Advisory Committee. It has also been reviewed by the Director of the Division of Epidemiology and Clinical Applications, NHBLI, and the Director, NHLBI.

6. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart, Lung, and Blood.

The NHLBI maintains extensive education programs directed toward prevention of cardiovascular disease through reductions in cardiovascular risk factors. Previous efforts have been targeted at specific risk factors without emphasizing intervention in the young. The NHLBI now recognizes the need for early development of dietary patterns that reduce cardiovascular risk factors and is presently developing a program in pediatric cardiology. In addition, the recent NIH Consensus Development Conference on Lowering Blood Cholesterol made specific recommendations for limitations on dietary fat and cholesterol levels for all individuals aged two and above.

7. Intended User: The intended users include the program administrators for the NHLBI efforts in pediatric cardiology and in nutrition and the prevention of cardiovascular disease, the Chief of the Prevention and Demonstration Research Branch of the Division of Epidemiology and Clinical Applications, the Director of the Division of Epidemiology and Clinical Applications, and the Associate Director for Prevention, Education, and Control, NHLBI.

   The survey results are expected to be available to the Institute by June of 1988.

8. Information to be Generated: In recent years, the concept that CHD prevention should start in childhood has attracted increasing attention. This is borne out by the statements and recommendations proposed by various expert committees and organizations (e.g., the Joint National Commission on Prevention and Control of Hypertension, the NIH Consensus Panel on Lowering Blood Cholesterol, the American Heart Association, etc.) which all advocated identification of the intervention in coronary heart disease (CHD) risk factors in childhood.

   It is possible to identify a number of potential barriers to prevention of CHD in the young. First, physicians caring for children may be particularly sensitive to the problem of early diagnostic labeling and its attendant psychological risks. There is, after all, no clear scientific evidence at the present time that modifying CHD risk factors in children leads to definite prevention of CHD in adulthood. Second, there is traditional antipathy toward dietary change for growing children who, due to their relatively high nutritional requirements, are particularly vulnerable to undernutrition. Third, there is also a tendency on the part of pediatricians and other primary care providers for children to view CHD as an adult-onset disease and, therefore, not an area of immediate concern for the young.

   Traditionally, those who provide health care for children have been in the forefront of innovative preventive care. What is not ascertained at present is whether or not those physicians caring for children are as receptive to the identification and treatment of CHD risk factors in the young as they are to the more traditional aspects of preventive medicine. The objectives of the study are as follows:

   1. To determine for a representative sample of pediatricians, family medical physicians, and general practitioners:

      a. their attitudes regarding the issue of starting CHD prevention in childhood;

      b. their views relevant to CHD prevention in the young, i.e., the identification of risk factors, screening, and diagnostic methods; awareness of the latest recommendations by various expert committees regarding detection and management of individual risk factors; the issues of "tracking" of CHD risk factors; and

      c. their current practice behavior in the area of CHD risk factor detection and modification.

2. To gather information to make recommendations for future educational and training programs which will promote greater effectiveness in the practice of cardiovascular disease prevention.

3. To provide information to enable the NHLBI to disseminate health research results more efffectively to health care providers caring for the young.

4. To collect and compile baseline data for future research of delivery of services for prevention of CHD in the young.

9. Approach: The survey will consist of telephone interviews with a representative sample of those physicians listed in current directories of such organizations as the American Academy of Pediatrics and the American Academy of Family Medicine, and, also, to those physicians in general medical practice as listed in the AMA directory. According to the latest published information (Pediatrics 74:991, 1984) approximately 57.6% of the children up to age 10 receive their care from pediatricians, 5.4% from family physicians, and 21% from general practitioners, accounting for 84% of children in this group. Between ages 10-14, pediatricians provide 25.5% of care, family physicians 6.4%, and general practitioners 33.0%. Therefore, the great majority of primary care providers to children can be reached by surveying these three specialty groups.

Non-respondents will be characterized by such variables as geographic location, age, and other demographic variables to determine whether they differ systematically from respondents. Similar previous survey experiences have shown that a modest fee for telephone questionnaire participants increases the response rate from physicians, so a fee of $25 per interview will be offered.

Included in the questionnaires will be items related to children of selected ethnic groups since there may be differences among ethnic groups in both risk status and unmet medical needs in the area of CHD prevention.

10. Information Clearance/Collection: Yes

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NHLBI 86-402

2. Project Title and Capsule Description:

   a. Title: Knowledge, Attitudes, and Behavior of Nurses and Dietitians Regarding Cardiovascular Risk Factors

   b. Capsule Description: Registered nurses and dietitians will be surveyed to determine their knowledge, attitudes, and behavior related to the three major modifiable cardiovascular risk factors: hypertension, elevated blood cholesterol, and cigarette smoking.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	($75)	-	($75)
87	($200)	-	($200)
88	($75)	-	($75)

Cost Justification: The projected costs are based on surveys of comparable content and scope conducted recently by the NHLBI. The FY 1986 costs are for survey design with the remaining FY 1987/1988 costs allocated to implementation and analysis. The NHLBI must rely upon contractors for the design and conduct of surveys since it has no such internal capability.

4. Project Monitor/Contact:

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5. Coordination: The project was reviewed by the Associate Director for Prevention, Education, and Control, NHLBI, and the NHLBI Coordinator for Nutrition; and nutritionists and statisticians within the Division of Epidemiology and Clinical Applications and the Division of Heart and Vascular Diseases.

6. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart, Lung, and Blood.

The Office of Prevention, Education and Control administers three of the major educational programs of the NHLBI; namely, the National High Blood Pressure Education Program (NHBPEP), the National Cholesterol Education Program (NCEP), and the NHLBI Smoking Education Program (NSEP).

Each of the programs was developed to inform health professionals, patients either with established cardiovascular or with cerebrovascular disease or cardiovascular risk factors, and the general public, of the cardiovascular risks associated with specific characteristics and behaviors, and also the need and methods available to reduce these risk factors.

7. Intended User: The program managers of the NHBPEP, NCEP, and NSEP will rely upon the results of this survey to provide baseline evaluation data and to revise and redirect professional education program efforts to meet the information needs of dietitians and nurses regarding cardiovascular risk factors and their modification. The information should be available to the intended users by February 1988.

8. Information to be Generated: The survey will provide the NHLBI with information pertaining to:

   a. the sources of information and information channels through which dietitians and nurses learn about cardiovascular risk factors and their modification,

   b. their current knowledge of the major cardiovascular risk factors and the extent to which the risk factors interact,

   c. their general beliefs and current practice relating to risk factor modification,

   d. the risk factor reduction strategies they presently employ, and

   e. their individual personal health practices relating to the modifiable cardiovascular risk factors.

9. Approach: A national sample of practicing dietitians and nurses will be surveyed. An initial mail questionnaire and cover letter will be sent to the selected nurses and dietitians. Those who do not return the questionnaire within a reasonable period of time will be sent a reminder postcard. If there is still no response, a follow-up phone call will be placed. All non-respondents will be characterized by variables such as location and age to help determine whether they differ in some respect from the survey respondents.

   Because the active nurses of the United States are engaged in a greater variety of practice settings than the active dietitians, it is expected that a substantially greater number of nurses will be surveyed. The exact sample size for each of the two subject professions will be determined in consultation with the contractor after discussions with the appropriate professional organizations have resulted in the identification of representative practice classifications.

   Since only 165,000 of the 1.4 million active registered nurses in the United States are members of the American Nurses Association (ANA), the sample of nurses will be drawn from state licensing agencies. Apart from the vast superiority in the relative completeness of the state licensing records, use of the state licensing records offers other significant advantages to the study. Geographic stratification will obviously be greatly facilitated and, since the records include data on the areas of specialization, coverage of nurses in a range of practice settings can be assured.

For dietitians, the membership records of the American Dietetic Association should provide a relatively complete source from which to sample. There are approximately 40,000 registered dietitians in the United States, most of whom are members of the ADA. The ADA does include within its records an indication of the kind of practice activity in which each member is engaged so that stratification by practice will be possible.

10. Information Clearance/Collection: Yes

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NHLBI 86-403 (Withdrawn)

2. Project Title and Capsule Description:

   a. Title: Evaluation of the Use of Nutrition Counseling Skills Publications

   b. Capsule Description: The project will assess the frequency of use, utility, and impact of publications emanating from NHLBI-supported programs developed to improve nutrition counseling skills among nutrition educators and counselors.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	($42)	-	($42)
87	($18)	-	($18)

4. Project Monitor/Contact:

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5. Coordination: This project was reviewed and awarded a high priority by the Clinical Applications and Prevention Advisory Committee of the NHLBI. It has also been reviewed by the Director, NHBLI.

6. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart, Lung, and Blood.

   National programs for the prevention and treatment of cardiovascular disease include efforts to change food habits. As these efforts continue to expand there will be a corresponding increase in the need for nutrition personnel trained in this specialty. The NHLBI was aware of this future need when it expended approximately $400 thousand to sponsor a series of experimental, regional workshops to improve the counseling skills and nutrition knowledge related to hyperlipidemia of practicing nutritionists and another $40 thousand to create and distribute the publications that resulted from the workshops.

   The experimental workshops were the subject of an earlier NHLBI evaluation project (NHLBI 80-307). The evaluation concluded that participant attitudes showed positive changes over the course of the workshops and that they gained in a variety of skills and techniques. However, the benefits of the workshop were only directly available to the 400 participants. As one result of the evaluation project, the Institute decided to prepare publications that would allow much wider dissemination of the workshop approach. The first of the two volumes provides guidance on how to design similar workshops while the second offers outlines of sample sessions. There are presently 55,000 members of the American Dietetic Association and approximately half of the membership are practicing educators or counselors. This evaluation will allow the NHLBI to determine whether the publications offer an effective mechanism for extending the positive experiences of the workshop participants to the remainder of the dietitian community. If so, then both the expenditures for preparing the publications and evaluating their utility will be found to be highly cost-effective. The benefits of the workshops will be available to the entire dietitian community at a unit cost dramatically below the unit cost for each workshop participant.

7. Intended User: The information developed by the project will aid the NHLBI in determining whether publications from the workshops are an effective approach for professional education among dietitians and whether they are used by practicing dietitians in designing counseling programs for their clients. If the approach is shown to be successful among dietitians it may then be extended to other health professionals. The evaluation will also provide an indication of areas where additional professional education programs for dietitians should be concentrated. The NHLBI National Cholesterol Education Program to be initiated in FY 1986 will also benefit from the information developed.

8. Information to be Generated: The project will develop information on the extent, frequency, and manner of use of the Institute publications, Building Nutrition Counseling Skills, Volumes I and II. In particular, users and recipients will be questioned regarding the relative utility of each of the two volumes, the extent to which the two volumes are used independently or jointly, and the subject areas that were either omitted, inadequately covered, too extensively covered, or included but could have been omitted. Data will also be collected on the educational settings and kinds of programs or courses in which the materials are used and the characteristics of users. In addition, individuals who received the materials but are not using them will be questioned on their reasons for not using the materials.

9. Approach: The publications were distributed by the NHLBI in January 1985 to all identifiable dietitian educators and dietetic intern program directors, to state nutrition directors, to the workshop participants, and to regional office nutritional consultants in the Public Health Service. In addition, single copies were sent by the Institute to individuals upon request. In all, approximately 2,250 copies of the publications were sent out by the NHLBI. The remainder of the 3,000 printed copies have been made available to interested parties through the Government Printing Office with a notice of their availability printed in leading journals in nutrition in May 1985. Unfortunately, the GPO does not maintain records of the individuals who request particular publications, so the study will be constrained to known recipients of the publications.

Questionnaires requiring approximately 20 minutes of respondent time will be distributed to each of the known recipients. Telephone follow-ups are planned for each individual who fails to respond within a reasonable period of time. A contractor will design and administer the survey instrument, analyze the collected results, and prepare a final report. Particular attention will be directed toward characterizing the answers by the primary work activity of the respondents. An attempt will be made to identify systematic differences between those to whom the publications were sent at the initiative of the NHLBI and those who received the publications in response to their direct requests to the NHLBI. In addition, an attempt will be made to note whether non-respondents differ from respondents in any important characteristics.

10. Information Clearance/Collection: Yes

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NHLBI 86-404

2. Project Title and Capsule Description:

   a. Title: Public Attitudes and Practice Regarding Cholesterol and Coronary Heart Disease

   b. Capsule Description: Public attitudes and practice regarding cholesterol and coronary heart disease will be assessed in the fall of 1986 and compared with results obtained in identical surveys conducted previously to determine the public impact of the results of the Coronary Primary Prevention Trial (CPPT) and the new National Cholesterol Education Program.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	($89)	($5)	($84)

Cost Justification: The data for this evaluation will be collected by adding our questions to the existing Food and Drug Administration (FDA) annual public survey. The NHLBI must rely upon contractors for the collection of survey data since the Institute has no in-house capacity for survey administration.

4. Project Monitor/Contact:

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(301) 496-1681

5. Coordination: This project was reviewed and approved by the NHLBI Arteriosclerosis, Hypertension, and Lipid Metabolism Advisory Committee and the Director of the Division of Heart and Vascular Disease.

The project is expected to be performed under an inter-agency agreement with the Consumer Research Staff of the Food and Drug Administration.

6. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart, Lung, and Blood.

The survey will allow the NHLBI to assess the public impact of the results of the Coronary Primary Prevention Trial, the single most costly research project supported by the NHLBI, and the new National Cholesterol Education Program which will parallel the National Hypertension Education Program in level of effort.

7. Intended User: The results of the survey will be used in conjunction with the companion earlier surveys conducted in the fall of 1983 and the fall of 1985 by FDA for the Division of Heart and Vascular Diseases to assess the impact of the CPPT announcement and by the Office of Prevention, Education, and Control to evaluate and refine their public educational campaigns.

8. Information to be Generated: Conduct of a second post-CPPT survey of public attitudes and behavior regarding cholesterol and coronary heart disease will allow the NHLBI:

   - To track changes in public response over time by comparing results of the survey to responses made in two previous surveys, one conducted just prior to and the other conducted two years after release of the CPPT results,

   - To estimate the impact of the CPPT on public behavior, and

   - To identify areas where continued public education is needed.

Major public health efforts are currently underway to reduce mortality and morbidity from CHD by reducing blood cholesterol through more aggressive treatment and through modest shifts in the dietary habits of the American public. The American Heart Association, the media, and food industry advertisements are already directing intensive cholesterol education messages to the public and a major educational effort coordinated by the NHLBI is in the planning stage.

These educational efforts are in response to very specific public health recommendations regarding blood cholesterol that were made by an expert panel convened at the NIH Consensus Development Conference on Lowering Blood Cholesterol to Prevent Heart Disease. The panel recommended that adults know their blood cholesterol levels and that they seek treatment if their blood cholesterol exceeds the 75th percentile for their age-and sex-specific group. As a preventive measure, the panel further recommended that the public make dietary changes to reduce the intake of dietary fat and cholesterol and to reduce the intake of total calories.

The Consensus panel recognized that changes would not be make quickly but rather, gradually, over time and that as the public adopts changes there will be concurrent changes in physician practice, changes in available treatments and changes in food marketing. The panel recommended that all of these changes be carefully monitored.

A follow-up of a previous NHBLI evaluation survey project, originally designed to assess the impact of the CPPT, can accomplish much of this monitoring. In the fall of 1983, just before the release of the results of the CPPT, the NHLBI surveyed the American public to determine attitudes, knowledge and habits regarding blood cholesterol. A resurvey will be conducted in the fall of 1985, using identical survey questions and methodology. The repeat survey will assess the effects of the considerable attention given blood cholesterol reduction, by the public media and professional publications and forums, since the announcement of the CPPT findings. The post-CPPT survey will also identify areas requiring continued educational emphasis.

The 1983 and the 1985 surveys are joint NHLBI - FDA efforts. They are extremely modest in cost and provide a valuable data base for the programs of both agencies, for the National Cholesterol Education Program of the NHLBI, and for the nutrition labeling program of the FDA. Others in biomedical/public health research, industry and voluntary agencies have also used the baseline data from the 1983 survey.

Judging from the results of the 1983 survey, the public will have to make significant health and diet changes to meet the recommendations set forth by the Consensus panel. In 1983, only one-third of adults thought their blood cholesterol levels had been checked and fewer than 5% knew their cholesterol level. About 5% had been treated by a physician for elevated blood cholesterol. Less than 15% had attempted diet changes, either self-initiated or M.D.-initiated, to control blood cholesterol. This public report of relatively low frequency of treatment was corroborated by results of an NHLBI physician survey. On average, physicians reported treating patients above the 95th percentile, indicating that only a small fraction of their patients were receiving advice about diet or drug therapy for blood cholesterol-lowering.

9. Approach: This proposal will provide for the administration of an additional public survey in the fall of 1986. The objective of the survey is to track changes in public behavior. Results will be compared with public responses made in the fall of 1983 and the fall of 1985. It is important to have frequent yearly assessments during this very dynamic period when so much information is being directed to the public from both reliable and less reliable sources. It is important to know whether the varied sources of information are creating an adverse impact by causing public confusion rather than increased public knowledge. The survey results can also be useful in interpreting results from other Lipid Metabolism-Atherogenesis Branch projects designed to monitor existing commercial data bases to assess changes in patterns of drug use and food distribution.

10. Information Clearance/Collection: Yes

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NHLBI 86-405

2. Project Title and Capsule Description:

   a. Title: Evaluation of Pulmonary Faculty Development Award

   b. Capsule Description: The impact of the Pulmonary Development Faculty Award will be assessed. Particular attention will be directed toward the development of pulmonary training at participating medical centers, the level of pulmonary research activities among the trainees, and the degree to which research and training capabilities are strengthened at the schools involved. The aim will be to examine the concept of the program, not the individual participants, in order to identify strengths and weaknessess of the program for future manpower initiatives.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	($30)	-	($30)

Cost Justification: Much of the data on research grant activity and publications can be developed internally, but supplementary information will be obtained as needed directly from the awardees, the faculty at the training centers, and/or the faculty at the medical schools that sponsored the pulmonary faculty trainees.

4. Project Monitor/Contact:

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5. Coordination: The project has been reviewed by the Chief of the Prevention, Education, and Research Training Branch and the Director of the Division of Lung Diseases.

6. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart, Lung, and Blood.

The pulmonary faculty development award was initiated by the NHLBI to develop research and training programs in pulmonary medicine by providing the opportunity for junior faculty in institutions without strong pulmonary research programs to spend an extended period of time pursuing pulmonary research at institutions with established pulmonary programs. The award provided salary and research support for a five-year period, three of which were to be spent at one of five participating training institutions with the remainder to be spent at the sponsoring institution. The awardees were required to agree to remain at the sponsoring institution for at least three years beyond the term of the award. For its part, the sponsoring institution was required to insure a full-time faculty position and support in time and resources for the awardees for a term of three years following completion of the award. Awards were made under the program from FY 1975 through FY 1980. Over that period, 33 awardees from 25 different sponsoring institutions participated in the program.

7. Intended User: The prinicipal users of the results will be the Director and staff of the Division of Lung Diseases. The results should also be useful to directors of other NIH programs that require trainees to leave their sponsoring institutions for training elsewhere and then return to the sponsoring institutions. Results of the evaluation should be available to the intended users by December 1986.

8. Information to be Generated: The project will provide information relevant to the following aspects of the program:

° pulmonary faculty development awardees	-	Measures will be developed to reflect the extent to which they have established successful careers in pulmonary research. Summaries will be prepared of the awardees views of the program, whether negative or positive. Particular emphasis will be placed upon those aspects of the program that the awardees indicated as contributing and/or failing to contribute to their career development.
° training institutions	-	Summaries will be prepared on the views of the training directors on the positive and negative aspects of the program and their recommendations for structuring similar programs in the future.
° sponsoring institution	-	Measures will be developed to reflect the extent to which active training and research programs in pulmonary medicine have been established at the sponsoring institutions. Summaries will be prepared of the views of departmental chairs of the sponsoring institutions regarding the ways in which the program contributed to development of pulmonary research and training in their institutions, the

actions that have been taken at the institution to promote the success of the program, and their recommendations for increasing the efficacy of similar programs in the future.

9. Approach: Several different approaches will be relied upon in evaluating the program.

  ° Data will be collected from available sources on grant applicant activity and publications/citations of awardees and several comparison groups. Some of the comparison groups that will be considered include approved but not paid PFDA applicants, RCDA awardees in lung programs, and recipients of the Pulmonary Academic Award. Comparisons will be made among the awardees and the other groups to assess research activity, significance of research, academic promotion, etc.

  ° Data will also be collected on the relative levels of pulmonary related grant activity at the sponsoring institutions before and after participation in the program. The receipt of training awards in pulmonary medicine will also be noted.

  ° A workshop will be conducted for awardees trained under the program to review and interpret some of the data collected and to obtain their perceptions of the positive and negative aspects of the program.

  ° On-site visits will be made to several of the sponsoring institutions where the pulmonary faculty development awardees have been successful in establishing active pulmonary programs and to several where there has not been as much progress in an effort to ascertain the contributing factors.

  ° A report will be prepared that will include an analysis of the findings and a summary of the recommendations.

10. Information Clearance/Collection: No.

Project No.: NHLBI 78-5

1. EDC ID No.: 1756

2. Entry Dates: 3. Status: Completed

4. Project Title: Evaluation of Progress in Pediatric Pulmonary Disease

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI 7. Start/End Dates: 78-06, 84-08

8. Performer: Outside Consultants; Institute Staff

9. Agency Contact: Gail, Dorothy; NIH, Westwood Building, Room 6A03; (301) 496-7171

10. Cost: FY 79-$3, FY 80-$23, FY 81-$1, FY 82-$18, FY 83-$5

11. Fund Source: Evaluation 12. Mechanism: In-house

13. Project No.: NHLBI 78-5 14. Contract No.: NA

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research, Child Development

20. Abstract: This project evaluated the progress made by the National Heart, Lung, and Blood Institute Pediatric Pulmonary Disease Program, since enactment of the Heart, Blood Vessel, Lung, and Blood Act of 1972. The Institute Program in Pediatric Pulmonary Diseases seeks to prevent cystic fibrosis, bronchiolitis, respiratory distress syndrome (RDS) and other pediatric pulmonary diseases and to improve the prognosis for patients with pediatric pulmonary conditions. The main questions addressed in this project were: (1) What progress was made in pediatric pulmonary disease in meeting the goals since 1972; (2) What directions or goals seemed appropriate for future development. During the first phase of the evaluation, a Steering Committee arrived at a consensus on the disease subcategories to be evaluated and a framework within which progress and needs could be assessed. Descriptive and judgmental information of progress, barriers to progress, needs and opportunities were obtained from 38 investigators and practitioners in pediatric pulmonary diseases. In phase II, the information was verified by a number of investigators, and summaries of the combined responses were prepared. The summaries were used by members of the Steering Committee and additional consultants in preparing a final report.

Project No.: NHLBI 79-304

1. EDC ID No.: 2086

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of the Effect of Sickle Cell Counseling

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 81-09, 86-02

8. Performer: Urban Behavioral Research Associates, 1204-6 Washington Blvd., Suite 100-210, St. Louis, MO 63103

9. Agency Contact: Gaston, Marilyn; NIH, Federal Building, Room 504; (301) 496-6931

10. Cost: FY 81-$90, FY 82-$91, FY 83-$90, FY 84-$174

11. Fund Source: Evaluation

12. Mechanism: Contract

13. Project No.: NHLBI 79-304

14. Contract No.: NO1-HB-1-3006

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research, Black Americans Social Attitudes and Public Opinion

20. Abstract: This project evaluates the effect of sickle cell counseling programs conducted as part of the National Sickle Cell Disease Program. The project focuses on the psychosocial effects of counseling related to counselees' feelings, attitudes and behavior.

The study is both prospective and longitudinal in design, relying on survey questionnaires, interviews and structured observation methodology. The data will be collected from federally funded Comprehensive Sickle Cell Centers and Screening and Education Clinics and will consist of three major types of information: (a) profiles of Centers and Clinics counseling programs--e.g., methodology, training, etc.; (b) information related to the counselees' feelings, attitude, behavior prior to, immediately after, and one year following counseling; and (c) information related to the counselor--e.g., his/her orientation and expectations for counseling, attitudes and feelings about sickle cell trait and disease.

Project No.: NHLBI 79-311

1. EDC ID No.: 1761

2. Entry Dates: 3. Status: Completed

4. Project Title: Evaluation of Regimen Compliance in Long-Term Clinical Trials

5. Report Title: Howard J, Whittemore AS, Hoover JJ, Panos M, and the Aspirin Myocardial Infarction Study Research Group: How Blind Was the Patient Blind in AMIS? Clin. Pharmacol. Ther. 32:543-553, 1982.

Mattson ME and Friedman LM: Issues in Medication Adherence Assessment in Clinical Trials of the National Heart, Lung, and Blood Institute. Controlled Clin. Trials 5:488-496, 1984.

Mattson ME, Curb JD, McArdle R, and the AMIS and BHAT Research Groups: Participation in a Clinical Trial: The Patients' Point of View. Controlled Clin. Trials 6:156-167, 1985.

Byington RP, Curb JD, Mattson ME for the Beta-Blocker Heart Attack Trial Research Group: Assessment of Double-Blindness at the Conclusion of the Beta-Blocker Heart Attack Trial. JAMA 253:1733-1736, 1985.

6. Agency Sponsor: PHS-NIH-NHLBI 7. Start/End Dates: 79-06, 84-09

8. Performer: Nancy Daub, University of Maryland, Department of Epidemiology and Preventive Medicine, 600 Wyndhurst Ave., Baltimore, MD 21210

9. Agency Contact: Friedmen, Lawrence; NIH, Federal Building, Room 216; (301) 496-4323

10. Cost: FY 79-$68, FY 80-$87

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NHLBI 79-311 14. Contract No.: N01-HV-5-2901

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research, Clinical Trials Feature

20. Abstract: This project evaluated patient and staff compliance in two long-term clinical trials of medications to prevent recurrent heart attacks [the Aspirin Myocardial Infarction Study (AMIS) and Beta Blocker Heart Attack Trial (BHAT) trials]. The evaluation focused on two facets of compliance: (1) the extent to which patients were taking their medication as prescribed and (2) the extent to which clinic staff were adhering to protocol in encouraging and measuring patient compliance. Phase one consisted of field data collection and phase two of a series of papers addressing issues of compliance.

The purpose of this project was to develop methods for determining the adequacy of the various measures of compliance used in the two trials (blood and urine tests, pill counts, patient representations, and staff assessments) and to apply these methods in evaluating compliance data routinely collected in the trials. Knowledge gained from the evaluation was used to improve the management of the BHAT trial, the analysis of data from both the AMIS and BHAT trials, and the design of future studies.

Project No.: NHLBI 80-304

1. EDC ID No.: 1763

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of the Statewide Hypertension Program

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 80-06, 86-09

8. Performer: Aurora Associates, Inc., 1140 Connecticut Avenue, N.W.,
Suite 1200, Washington, D.C. 20036; (202) 463-0950

9. Agency Contact: King, Cecile; NIH, Building 31, Room 5A11;
(301) 496-3620

10. Cost: FY 80-$18, FY 81-$34, FY 82-$21, FY 83-$207, FY 84-$66, FY 85-($258)

11. Fund Source: Evaluation

12. Mechanism: In-house; Contract

13. Project No.: NHLBI 80-304

14. Contract No.: N01-HO-3-7007

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Insitute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Heart Disease, Program Coordinator

20. Abstract: The Statewide Hypertension Coordination Program was initiated in response to a Congressional mandate to determine whether coordination of state activities related to hypertension detection and control could cause major changes not only in hypertension status but also in the morbidity and mortality of diseases linked to elevated blood pressure. In 1978, four states (Connecticut, Maryland, South Carolina, and California) received funding from the Institute as part of this program. Three other states (Michigan, Georgia, and Maine) joined the program in 1980.

The contractor is comparing and contrasting the State evaluation activities across the seven program states. An interim summary analysis of the first four states is planned and an analysis of hypertension coordination activities across selected non-program and program states will be performed to evaluate the effect of the Statewide program on state hypertension control organization. In addition, the contractor will analyze National trends in hypertension control during the period of the statewide program.

Project No.: NHLBI 80-310

1. EDC ID No.: 1768

2. Entry Dates:

3. Status: In-process

4. Project Title: Assessment of Reach and Frequency of High Blood Pressure Messages

5. Report Title: None

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 81-09, 87-09

8. Performer: Broadcast Advertisers Reports, 500 Fifth Ave
New York, NY 10036

9. Agency Contact: Bellicha, Terry; NIH, Building 31, Room 4A31;
(301) 496-4236

10. Cost: FY 82-$48, FY 83-$47, FY 84-$50, FY 85-($45), FY 86-($45), FY 87-($45)

11. Fund Source: Evaluation, Program

12. Mechanism: Contract

13. Project No.: NHLBI 80-310

14. Contract No.: 263-82-C-0021

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Other

19. Descriptors: Media, Heart Disease

20. Abstract: The National High Blood Pressure Education Program uses a variety of mechanisms to increase public and professional awareness of the dangers of hypertension and ways of treating the problem. The electronic media are used extensively in the program. A key factor in the effectiveness of this approach is the extent to which the messages are aired. In order to evaluate this factor on a nationwide basis, this project is monitoring on a periodic basis the airing of messages across the country. Data are obtained from a commercial monitoring service. With the radical changes that are occurring in the electronic media, such as cable and satellite broadcasts, this actual use data has become of greater interest and importance for future time and fund allocation.

The primary application of the results will be to guide NHBPEP planning and resource allocation for its television public service messages, in which the Institute has a high investment. The market-by-market analysis of monitoring data will be used to assess message placement strategies and to identify those markets in which the Program needs to intensify efforts to place messages with stations. Audience reached and frequency of exposure to high blood pressure messages will be analyzed in relation to other Program evaluation activities, especially Health Message Testing Service results and current data from surveys on high blood pressure awareness and behavior.

Project No: NHLBI 81-313

1. EDC ID No.: 2012

2. Entry Dates:

3. Status: Completed

4. Project Title: Evaluation of the Framingham and other CHD Risk Models in a Large National Cohort-Phase I

5. Report Title: None (Final Report will be submitted under NHLBI 84-402)

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 81-05, 84-06

8. Performer: National Center for Health Statistics; National Institute on Aging

9. Agency Contact: Millicent Higgins;NIH, Federal Bldg., Room 2C-08; (301) 496-2327

10. Cost: FY 81-$100

11. Fund Source: Evaluation

12. Mechanism: Interagency Agreement

13. Project No.: NHLBI 81-313

14. Contract No.: Y01-HV-10047

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Research and Data Development

19. Descriptors: Statistical Data Feature, Heart Disease

20. Abstract: Since its inception, the NHLBI has devoted a substantial proportion of its research efforts to the delineation and quantification of risk factors for the development of coronary heart disease. The importance of Framingham and other longitudinal studies (most of which have been conducted with support from the Institute) in determining national health policy for the primary prevention or delayed onset of coronary heart disease are well known. This project examined the applicability of the Framingham-derived model in predicting coronary heart disease for the U.S. population as a whole.

The project was able to capitalize upon a follow-up study being organized and conducted by the National Center for Health Statistics (NCHS) in collaboration with the National Institute on Aging (NIA). The survey attempted to locate and determine the health status of all 15,500 adults in the original Health and Nutrition Examination Survey (HANES) cohort conducted in 1971-74. This provided an excellent opportunity to evaluate the utility of major predictive models (such as Framingham) of coronary heart disease in a large probability sample of the U.S. population in which serum cholesterol and other major variables were initially collected in a standardized manner. The survey has been completed.

Project No.: NHLBI 82-308

1. EDC ID No.: 2008.1

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of a Demonstration Program for Hypertension Control Using Community Health Centers: Phase II

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 82-02, 86-12

8. Performer: Evaluation Technologies, 2020 North 14th Street, Suite 620
Arlington, Virginia 22201

9. Agency Contact: Payne, Gerald; NIH, Federal Building, Room 6A08;
(301) 496-2465

10. Cost: FY 82-$1, FY 83-$156, FY 84-$199, FY 85-($153)

11. Fund Source: Evaluation

12. Mechanism: In-house; Contract

13. Project No.: 82-308

14. Contract No.: N01-HC-38003

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH Biomedical Research-Institute Specific-National Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Demonstration Project Heart Disease, Community Health Centers

20. Abstract: This project is evaluating one of several efforts related to the dissemination of the results of a recently completed NHLBI clinical trial, the Hypertension Detection and Follow-up Program (HDFP). The effort is a demonstration of a hypertension control program in community health center settings. This project is the second phase of the evaluation, the Conduct of the Evaluation. The first phase, Planning, is nearly completed. The results of the evaluation are expected to identify how much of the HDFP protocol can be implemented in an existing health care system and whether the approach is economically feasible.

Project No.: NHLBI 83-403

1. EDC ID No.: 2401

2. Entry Dates: 3. Status: Completed

4. Project Title: Assesssment of the Collection, Processing, and Use of Blood Resources

5. Report Title: Assessment of the Collection, Processing, and Use of Blood Resources

6. Agency Sponsor: PHS-NIH-NHLBI 7. Start/End Dates: 84-06, 85-07

8. Performer: Professional Management Associates
15825 Shady Grove Rd., Suite 190
Rockville, Maryland, 20850

9. Agency Contact: Czarra, Allan W.; NIH, Federal Building, Room 520; (301) 496-4186

10. Cost: FY 84-($50)

11. Fund Source: Program 12. Mechanism: Contract

13. Project No.: NHLBI 83-403 14. Contract No.: N01-HB-47000

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Research and Data Development

19. Descriptors: Blood Bank, Statistical Data Feature

20. Abstract: Continued collection and analysis of data on blood resources are required to assess the effects of current blood resources research programs and to plan future research directions. Previous data collection efforts were forced to rely upon surveys of the blood services community because no relevant data bases existed. The advent of prospective reimbursement programs and standardization in health provider billing and reporting, provides the Institute with an opportunity to plan for the use of these standardized systems as blood resources data sources. This project identified the ways in which the new data systems can be used and specified the ways in which they can be modified to meet the future information needs of the Institute.

Project No.: NHLBI 83-405

1. EDC ID No.: 2402

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluability Assessment of the Minority Hypertension Research Development Summer Program

5. Report tle: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 84-06, 85-12

8. Performer: Birch and Davis Associates, Inc.
8905 Fairview Road, Suite 300
Silver Spring, Maryland 20910

9. Agency Contact: Hayden, George; NIH, Federal Building, Room 3A10; (301) 496-1724

10. Cost: FY 84-($130)

11. Fund Source: Program

12. Mechanism: Contract

13. Project No.: NHLBI 83-405

14. Contract No.: N01-HV-48074

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Biomedical Research, Heart Disease, Scientific Manpower, Minority Groups

20. Abstract: The Minority Hypertension Research Development Summer Program provides minority institution faculty members and graduate students with the opportunity for research development in the area of hypertension. Awards are made to training centers with well established hypertension research activities to expose selected faculty members and graduate students from minority institutions to the latest clinical and basic research on hypertension and to hypertension-related prevention and education programs. This evaluation project will:

(1) Identify the objectives of the program in the views of the NHLBI, the training centers, the participating minority institutions, and the trainees.

(2) Examine the appropriateness of the program design.

(3) Develop measures of progress toward the objectives and construct a process of data collection and reporting to enable the program to measure progress.

(4) Assemble the relevant available information on program operation and impact to provide an assessment of the program to data.

Project No.: NHLBI 84-402

1. EDC ID No.: 2371

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of the Framingham and Other CHD Risk Models in a Large National Cohort: Phase II--Supplementary Data Collection and Analysis

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 84-03, 85-09

8. Performer: National Center for Health Statistics

9. Agency Contact: Millicent Higgins; NIH, Federal Building, Room 2C08; (301) 496-2327

10. Cost: FY 84-($150)

11. Fund Source: Program

12. Mechanism: Transfer

13. Project No.: NHLBI 84-402

14. Contract No.: 1-Y01-HV-40047

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Research and Data Development

19. Descriptors: Statistical Data Feature, Heart Disease

20. Abstract: The purpose of this study is to evaluate the accuracy of predictive models relied upon by the NHLBI in making programmatic decisions and in designing and funding its prevention programs. When coupled with the original Health and Nutrition Examination Survey (HANES) conducted between 1971 and 1974, the present HANES follow-up survey will provide an independently obtained national probability sample of 15,500 individuals who were 35 years or older at the time of the original survey and for whom initial data on serum cholesterol and other major variables were collected in a standardized manner. In the follow-up survey, surviving participants of the original survey are being interviewed to obtain a detailed medical history and examined for blood pressures and body weights. Death certificates and relevant health information on decedents are being collected wherever possible. The NCHS will apply the Framingham risk models for heart disease and stroke morbidity and mortality, and other NHLBI predictive models for heart and lung diseases to data collected in the original HANES survey between 1971 and 1974. The predicted ten year morbidity and mortality will then be compared with the actual morbidity and mortality experience of the original HANES participants. NCHS participation in the study ensures an independent review of NHLBI program decisions and public dissemination of the results.

Project No.: NHLBI 84-404

1. EDC ID No.: 2372

2. Entry Dates:

3. Status: In-process

4. Project Title: Programmatic Evaluation of Behavioral Approaches to Treatment of Hypertension

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 84-02, 86-07

8. Performer: Institute Staff; Omar McCall and Associates, 11325 Maryland Avenue, Suite A, Beltsville, Maryland, 20705

9. Agency Contact: Kaufman, Peter; NIH, Federal Building, Room 604; (301) 496-9380

10. Cost: FY 84-($130), FY 85- ($110), FY 86-($150)

11. Fund Source: Program

12. Mechanism: In-house; Contract

13. Project No.: NHLBI 84-304

14. Contract No.: N01-HC-48075

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Research and Data Development

19. Descriptors: Heart Disease, Statistical Data Feature

20. Abstract: Pilot studies have demonstrated the ability of non-pharmacological therapies to achieve blood pressure decreases with some patients as well as suggesting their utility for maintaining pharmacologically lowered pressure or allowing a lower drug dose.

The objectives of this evaluation project are to expand the information available from current limited research efforts on non-pharmacological treatments and pursue the implications of large scale Institute trials which suggest the need to explore more fully the feasibility of non-pharmacological therapies for hypertension.

This project will develop a data base that will track and analyze the results of programs funded through NHLBI on non-pharmacological approaches to the treatment of hypertension. The data base will be used by the Behavioral Medicine Branch to evaluate the effects of research it is currently supporting within the National Plan area of hypertension treatment and guide future re-

source allocation in the area. Information from the evaluation will (a) assess the effectiveness of cooperating biobehavioral projects (most of which are NHLBI supported), (b) suggest the most promising treatment approaches for defined patient populations, and (c) contribute to determining the appropriateness and feasibility of a controlled trial of non-pharmacological therapies for hypertension.

Project No.: NHLBI 84-405

1. EDC ID No.:

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of the Impact of the Coronary Primary Prevention Trial (CPPT) and Multiple Risk Factor Intervention Trial (MRFIT) on Clinical Practice: Measurements of Practice After Release of Clinical Trial Results

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 85-10,86-01

8. Performer: National Capitol Systems, Inc., 1900 L Street, N.W., Washington, D.C. 20036

9. Agency Contact: Schucker, Beth; NIH, Federal Building, Room 401; (301) 496-1681

10. Cost: FY 85-($200)

11. Fund Source: Program

12. Mechanism: Contract

13. Project No.: NHLBI 84-405

14. Contract No.: N01-HV-58082

15. NTIS No.: X-NYD

16. ERIC No.:

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research, Heart Disease, Clinical Trials Feature, Preventive Health Care, Survey or Questionnaire Feature, Statistical Data Feature

20. Abstract: Clinical trials have been and continue to be a major programmatic focus of the NHLBI. The Coronary Primary Prevention Trial (CPPT) was the single most costly trial ever supported by the NHLBI. Both the scale and expense required by primary prevention trials and the possible clinician skepticism concerning the importance of some coronary heart disease risk factors serve to underscore the importance of an impact evaluation of the CPPT. With the completion of the present study the NHLBI will be able to assess the impact of the CPPT trial on physician beliefs, knowledge, and practice regarding Coronary Heart Disease risk factors in general and cholesterol levels in particular. A sample of practicing physicians will be surveyed regarding sources of information that influence clinical practice with respect to coronary heart disease (CHD) risk factors. The results of this survey will be compared with those of a similar survey performed under Evaluation Project 82-302. The earlier survey was completed prior to the release of the CPPT trial results in January 1984.

Project No.: NHLBI 84-406

1. EDC ID No.: 2369

2. Entry Dates:

3. Status: In-process

4. Project Title: Evaluation of the Impact of the Coronary Primary Prevention Trial (CPPT) on Public Attitudes, Knowledge, and Behavior Regarding Serum Cholesterol and Other Risk Factors for Coronary Heart Disease (CHD)

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 84-01, 85-09

8. Performer: Food and Drug Administration, Consumer Research Staff; Institute Staff

9. Agency Contact: Schucker, Beth; NIH, Federal Building, Room 402; (301) 496-1681

10. Cost: FY 84-($75), FY 85-($84)

11. Fund Source: Research

12. Mechanism: Transfer; In-house

13. Project No.: NHLBI 84-406

14. Contract No.: Y01-HV-40007; Y01-HV-50044

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research, Heart Disease, Clinical Trials Feature, Preventive Health Care, Survey or Questionnaire Feature, Statistical Data Feature

20. Abstract: The data for this evaluation are being collected by adding NHLBI questions to the existing Food and Drug Administration (FDA) annual public survey. Identical surveys are planned for before (baseline) and after announcement of the CPPT results in January 1984 to:

- develop a profile of public awareness concerning serum cholesterol as a coronary heart disease risk factor,

- provide indications of public educational needs regarding cholesterol and its relation to diet,

- identify effective channels for communicating public health information, and

- estimate possible changes in public attitudes and/or behaviors regarding attempts to modify serum cholesterol that may be attributable to the CPPT outcome.

NHLBI program managers and policy makers will rely upon the results of the baseline public survey in designing dissemination programs for results of the CPPT. By comparing the baseline survey and follow-up survey results, program managers will be able to assess the impact on public attitudes and behavior of such costly clinical trials as the CPPT.

Project No.: NHLBI 85-401

1. EDC ID No.:

2. Entry Dates: 3. Status: In-process

4. Project Title: Survey of Physician Practice Behaviors Related to the Prevention of Lung Diseases

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI 7. Start/End Dates: 85-09, 87-09

8. Performer: Joan S. Cwi; Survey Research Associates, Inc., Baltimore, Maryland

9. Agency Contact: Wolle, Joan; NIH, Westwood Building, Room 6A10A; (301) 496-7668

10. Cost: FY 85-($198), FY 86-($0)

11. Fund Source: Program 12. Mechanism: Contract

13. Project No.: NHLBI 85-401 14. Contract No.: N01-HR-56025

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Research and Data Development

19. Descriptors: Preventive Health Care, Lung Disease, Statistical Data Feature

20. Abstract: The intent of this project is to survey a sample of physicians, including primary care, internal medicine, preventive medicine, and pulmonary medicine specialists, to determine their practices related to the prevention of lung diseases. The survey will specifically address the use of lung function tests, the interpretation of such tests, decisions to refer or to treat, the frequency with which occupational histories are taken, and the frequency with which smoking cessation counseling is provided. The survey will provide baseline data to be used in assessing the impact of a seven and one-half year, $21 million clinical trial initiated by the NHLBI in FY 1984 on early intervention for chronic obstructive pulmonary disease among smokers with mildly abnormal pulmonary function. It will also provide baseline data for physician education efforts of the NHLBI.

Project No.: NHLBI 85-402

1. EDC ID No.:

2. Entry Dates:

3. Status: In-process

4. Project Title: Assessment of the Role and Impact of Specialized Centers of Research (SCORs)

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 85-03, 87-09

8. Performer: NHLBI/OPPE

9. Agency Contact: Roth, Carl; NIH, Building 31, Room 5A11; (301) 496-3620

10. Cost: FY 86-($50)

11. Fund Source: Program

12. Mechanism: Internal; Contract

13. Project No.: NHLBI 85-402

14. Contract No.: X-NYD

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research

20. Abstract: The NHLBI Specialized Centers of Research Programs (SCORs) are large center grant programs directed toward research in areas of recognized need. Each of the individual Centers in a SCOR program is intended to provide a coordinated, multi-disciplinary approach to problems associated with the etiology, pathogenesis, diagnosis, treatment, and/or prevention of the condition on which the program is focused. Individual SCORs are expected to include both basic and human clinical research and reflect a central theme. In the aggregate, the individual SCORs in a program are expected to comprise a collective program that is coordinated by the NHLBI. A number of senior researchers with interests in areas currently receiving SCOR program support, working with the Extramural Division Directors of the NHLBI and the Associate Director of the Institute for Scientific Program Operation developed the following list of criteria, all of which they believed should be met before continuing SCOR program support in a research area: (1) The program is making progress toward achieving its stated goals; (2) Goals are proposed that represent a significant national need; (3) Other mechanisms of support are not meeting the goals; (4) The coordination of basic and clinical research has and will

continue to lead to productive interaction; (5) The environment has attracted talented investigators and lent itself to the development of skilled multi-disciplinary teams; (6) The coordination of basic and clinical research efforts has accelerated progress and there is evidence that this will continue; and (7) Collaboration between existing centers has been demonstrably productive. At present the NHLBI does not have an established methodology for examining each of the criteria for its several SCOR programs. This project will develop measures for each of the criteria that will assist the Director, NHLBI and the Directors of the Extramural Divisions in determining whether to continue existing SCOR programs and in selecting alternative areas for SCOR support. The methodology developed should also provide a guide for assessing centers programs for the other components of NIH that sponsor major centers programs.

Project No.: NHLBI 85-403

1. EDC ID No.:

2. Entry Dates: 3. Status: In-process

4. Project Title: Transfusion Medicine Academic Award (TMAA) Program Evaluation

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI   7. Start/End Dates: 84-11, 90-11

8. Performer: Charles W. Dohner, University of Washington, Seattle, Washington

9. Agency Contact: Parker, Christine; NIH, Federal Building, Room 518; (301) 496-4186

10. Cost: FY 85-($51), FY 86-($48), FY 87-($51), FY 88-($55), FY 89-($30)

11. Fund Source: Program   12. Mechanism: In-house; Contract

13. Project No.: NHLBI 85-403   14. Contract No.: N01-HB-57006

15. NTIS No.: X-NYD   16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Program Evaluation

19. Descriptors: Blood Bank, Curriculum Development

20. Abstract: The Transfusion Medicine Academic Award (TMAA) was initiated in January 1983 to (1) encourage the development of curricula in transfusion medicine, and (2) allow the awardees to broaden their expertise in transfusion medicine. The TMAA is a mechanism for supporting individuals and schools who together will make a committment to develop more effective programs in Transfusion Medicine. The Award provides 5 years of support to a Program Director, while he or she develops a teaching and research environment in transfusion medicine for students and physicians. This project will assemble baseline data on medical student knowledge and interest related to transfusion medicine and the coverage of transfusion medicine topics in medical school curricula. It will also establish a program monitoring system that will permit informed decisions regarding program modifications during its term and collect data necessary for an assessment of program effectiveness and impact. Each awardee institution will perform its own data collection and questionnaire administration. The data will then be forwarded to a contracted coordinating center so that comparative summaries can be developed and returned to the separate institutional participants for their own internal evaluations. The NHLBI will also be provided with the analytical results.

Project No.: NHLBI 85-404

1. EDC ID No.:

2. Entry Dates:

3. Status: In-process

4. Project Title: Analysis of Antihypertensive Drug Prescriptions

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NHLBI

7. Start/End Dates: 85-07, 85-12

8. Performer: Staff

9. Agency Contact: Haines, Carol; NIH, Building 31, Room 4A18;
(301) 496-1051

10. Cost: FY 85-($1)

11. Fund Source: Program

12. Mechanism: Contract

13. Project No.: NHLBI 85-404

14. Contract No.: In house

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood

18. Evaluation Type: Research and Data Development

19. Descriptors: Medical Practice, Statistical Data Feature

20. Abstract: A trend analysis of the antihypertensive medication prescribing patterns of physicians will be developed. Data from the time period 1968-1978 have already been gathered; data from 1979 through 1984 will now be obtained. The Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure has released two reports (JNC II in 1980 and JNC III in 1984) that have provided guidelines for the "stepped-care" treatment of high blood pressure. The National Disease and Therapeutic Index (NDTI) data to be obtained will allow a determination of the anti-hypertensive drugs -- whether alone or in combination -- that are being prescribed by physicians. Drugs will be grouped into their appropriate "steppedcare" classification (based on guidelines in JNC II and JNC III) and physician prescribing practices will be evaluated in light of the JNC recommendations. Trends in prescribing patterns will be identified. For example, changes in the use of diuretics and beta-blockers for hypertensive patients will be related to the release of data from clinical trials. Changes in prescribing patterns that followed the release of JNC II will be assessed and baseline data on practices at the time of the release of JNC III in May of 1984 will be collected.

Project No.: NHLBI 85-405

1. EDC ID No.:
2. Entry Dates:
3. Status: In-process
4. Project Title: High Blood Pressure: 1986 Survey of Physicians' Knowledge, Attitudes, and Reported Behavior
5. Report Title: X-NYD
6. Agency Sponsor: PHS-NIH-NHLBI
7. Start/End Dates: 85-09, 87-12
8. Performer: Birch and Davis Associates, Inc.; 8905 Fairview Road, Suite 300; Silver Spring, Maryland 20910
9. Agency Contact: Roccella, Edward; NIH, Building 31, Room 4A18; (301) 496-1051
10. Cost: FY 85- ($74), FY 86- ($251)
11. Fund Source: Program
12. Mechanism: Contract
13. Project No.: NHLBI 85-405
14. Contract No.: N01-HO-59000
15. NTIS No.: X-NYD
16. ERIC No.: NA
17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Heart Lung and Blood
18. Evaluation Type: Program impact
19. Descriptors: Medical Practice, Heart Disease, Statistical Data Feature
20. Abstract: In 1977 the NHLBI supported a nationwide survey of physicians' knowledge, attitudes, and reported behavior related to the diagnosis and management of hypertension. Since the 1977 survey, two reports of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure have been released (JNC II in 1980 and JNC III in 1984) that have provided new recommendations for the stepped-care management of high blood pressure. It is presently not known the degree to which physicians are following the recommendations. Other developments in hypertension since 1977 include the release of clinical trial results indicating the benefits of treating mild hypertensives, the spread of nondrug therapies for hypertension, and revision of the definition of hypertension. The proposed follow-up survey, to be conducted in 1986, will allow an assessment of changes in physicians' knowledge, attitudes, and reported behaviors since 1977. A representative, random sample of physicians who manage hypertensive patients, including general and family practitioners, internists, cardiologists, and nephrologists, will be surveyed. The survey instrument will be similar to the 1977 instrument, but will be updated to reflect new management approaches, including new antihypertensive drugs and nonpharmacological methods, and to address approaches to special population groups such as black hypertensives and renal patients.

7

NATIONAL INSTITUTE ON AGING

Dr. T. Franklin Williams, Director

Contents

List of Projects and Proposed Budget 7.3

Evaluation Documentation Center Forms for Continuing and Recently Completed Projects 7.5

National Institute on Aging Proposed Budget

		$ in Thousands		
		FY 85	FY 86	FY 87
NIA 83-301	Evaluation of the Progress and Potential Cost-Effectiveness of the NIA's Research Program in Senile Dementia of the Alzheimer's Type (SDAT), Component I (Effectiveness Study)	--	(33)	--
NIA 85-401	Evaluation of Research Training and Career Development Programs in Gerontology and Geriatrics	--	(NYD)	--
Total FY 86 NIA Evaluation Fund Request			(33)	

Note:

( ) non set-aside funds

1. EDC ID No.: 2368 Project No.: NIA 83-301

2. Entry Dates: 3. Status: In process

4. Project Title: Evaluation of the Research Program in Alzheimer Disease (AD), [formerly known as Senile Dementia of the Alzheimer's Type SDAT)] - Component 1 (Effectiveness Study)

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIA 7. Start/End Dates: 84-06, 86-09

8. Performer: Associate Consultants, Inc.
1701 K Street, N.W.
Suite 501
Washington, D.C. 20006

9. Agency Contact: Dr. Zaven Khachaturian, Bldg. 31, Rm. 5C-27, 496-9350

10. Cost: FY 84 - $75, FY 85 - ($0), FY 86 - ($33)

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIA 83-301 14. Contract No.: 263-84-C-0287

15. NTIS No.: NYD 16. ERIC No.: Not applicable

17. Program(s) Evaluated: PHS-NIH-Biomedical Research Institute (Specific Aging)

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Research and Evaluation Performance

20. Abstract: The purpose of this evaluation is to determine the effectiveness of NIA's program development in AD research in terms of success in stimulating meaningful research in this area, supporting the most crucial areas of study, and overcoming research obstacles posed by the unique characteristics of this disease. The outcome of this evaluation will be used to refocus the Institute's program as indicated.

1. EDC ID No: 2368 Project No. NIA 83-301

2. Entry Dates: 3. Status: Completed

4. Project Title: Evaluation of the Research Program in Alzheimer Disease (AD), [formerly known as Senile Dementia of the Alzheimer's Type (SDAT)] - Component 2 (Social/Economic Cost Study)

5. Report Title: See list of papers below.

6. Agency Sponsor: PHS-NIH-NIA 7. Start/End Dates: 83-09, 84-09

8. Performer: Applied Systems Institute, Inc., 1910 K Street, N.W., Suite 501, Washington, D.C. 20006

9. Agency Contact: Dr. William Cartwright, Federal Bldg., Rm. 612, 496-1178

10. Cost: FY 83 - $74

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIA 83-301 14. Contract No.: NO1-HE-3-2123

15. NTIS No.: NYD 16. ERIC No.: Not applicable

17. Program(s) Evaluated: PHS-NIH-Biomedical Research Institute (Specific Aging)

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Research and Evaluation Performance

20. Abstract: The purpose of this evaluation was to determine the effectiveness of NIA's program development in AD research in terms of success in stimulating research in this area, supporting crucial areas of study, and overcoming research obstacles posed by the unique characteristics of this disease. The outcome of this evaluation will be used to refocus the Institute's program, as necessary. This phase (Component 2) has examined the incidence and prevalence of AD in the U.S. and the economic costs associated with it. Related issues and recommendations have also been developed.

List of papers generated by this evaluation study:

1. Huang, L., Hu, T., and Cartwright, W. S. The Economic Cost of Senile Dementia in the United States, 1983. Submitted for publication in Medical Care.
2. McDonnell, N. S., Hu, T., and White, L. R. A Review of Prevalence and Incidence of Senile Dementia Among the Elderly Population. National Institute on Aging, 1984.
3. Hu, T., Huang, L., and Cartwright, W. S. Evaluation of Costs of Caring for Senile Demented Elderly: A Pilot Study. To be published in The Gerontologist, Summer, 1985.
4. Cartwright, W. S., Hu, T., and Huang, L. Cost of Illness and Elderly. Presented at the Atlantic Economic Conference, San Juan, Puerto Rico, March, 1984.
5. Cartwright, W. S., Hu, T., and Huang, L. Economic Costs of Senile Dementia: Issues and Recommendations. National Institute on Aging, 1984.

1. EDC ID No.:

Project No.: NIA 85-401

2. Entry Dates:

3. Status: In process

4. Project Title: Evaluation of Research Training and Career Development Programs in Gerontology and Geriatrics

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIA

7. Start/End Dates: 85-06, 86-11

8. Performer: Initial work will be performed by in-house staff.

9. Agency Contact: Alfred E. Burke, NIH Bldg. 31, Rm. 5C11, 496-4996

10. Cost: FY 85-($0); FY 86-(NYD)

11. Fund Source: S&E and evaluation fund for last phase

12. Mechanism: Internal and contract

13. Project No.: NIA 85-401

14. Contract No.: NYD

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS, NIA Research Activity Training, other relevant Department programs (i.e., PHS-ADAMHA Mental Health Training to be decided and agreed upon later)

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Research and Evaluation Performance

20. Abstract: The House Committee on Appropriations requested, in FY 1984, certain pertinent information about the training activities supported by DHHS in geriatrics and gerontology, e.g., how to improve and expand these activities. A report was submitted to Congress in February 1985, which responded to the Appropriation Committee's concerns and suggested the need to develop more definitive information on results of DHHS-supported training activities in geriatrics and gerontology, thus initiating the current evaluation efforts. From these efforts, it is anticipated that information will be ascertained concerning the effectiveness with which the Department is helping to provide needed personnel for the field of aging. This initial effort will concentrate on the field of aging research. A variety of analytical techniques are anticipated to be used including review of previous studies, surveys, bibliometrics research, etc. The types of data collected include current responsibilities of DHHS-supported fellows and trainees, their current assignments, sources of financial support, publications and other products of their activities, information on their career development plans, and other information. It is anticipated that several DHHS agencies will be involved, eventually, in the effort although this initial effort will include the NIA training programs.

8

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

Dr. Mortimer B. Lipsett, Director

Contents

List of Projects and Proposed Budget 8.3

Evaluation Documentation Center Forms for Continuing and Recently Completed Projects 8.5

National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases: Proposed Budget

	$ in Thousands		
	FY 85	FY 86	FY 87
NIADDK 85-401 Study of Obesity Research Awards	(2)	(3)	

Total FY 86 NIADDK Evaluation Fund Request (3)

Notes

( ) = non set-aside funds

1. EDC ID No.: Project No.: NIADDK 85-401

2. Entry Dates: 3. Status: In Process

4. Project Title: Study of Obesity Research Awards

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIADDK 7. Start/End Dates: 85-08, 85-12

8. Performer: OPPE, NIADDK, NIH
Bethesda, Maryland 20205

9. Agency Contact: Gonda, John R.; OPPE, NIADDK, Bldg. 31, Rm. 9A19
Bethesda, Maryland 20205

10. Cost: FY 85 - NA; FY 86 - NA

11. Fund Source: S & E 12. Mechanism: In-house

13. Project No.: NIADDK 85-401 14. Contract No.: NA

15. NTIS No.: NYD 16. ERIC No.: NA

17. Program(s) Evaluated:
PHS-NIH-Biomedical Research-Institute Specific- Arthritis, Diabetes, and Digestive and Kidney Diseases

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research

20. Abstract: A Consensus Development Conference on the Health Implications of Obesity was held at NIH in February 1985. As part of the planning for this conference, it was decided to take the recommendations of the Consensus Development Conference Panel and survey the obesity-related research award portfolio at NIADDK, with a view to comparing it with the recommendations of the Panel. The aim will be to assess the coverage and scope of the existing program and to identify areas that have not been explored yet in great depth.

9

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Dr. Anthony S. Fauci, Director

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List of Projects and Proposed Budget 9.3

Evaluation Documentation Center Form for Continuing Project 9.5

National Institute of Allergy and Infectious Diseases: Proposed Budget

		In Thousands		
		FY 85	FY 86	FY 87
NIAID-82-301	Evaluation of Decision Analysis Model Systems for the Accelerated Development of New Vaccines Program (ADNVP)	--	--	--
Total FY 86 NIAID Evaluation Fund Request			$0	

1. **EDC ID No.:** 2132 **Project No.:** NIAID 82-301
2. **Entry Dates:** 3. **Status:** In Process
4. **Project Title:** Evaluation of decision analysis model systems for the Accelerated Development of New Vaccines Program
5. **Report Title:** New Vaccine Development Establishing Priorities (Vols. I & II)
6. **Agency Sponsor:** PHS-NIH-NIAID 7. **Start/End Dates:** 82/09,85/06
8. **Performer:** Institute of Medicine, 2101 Constitution Ave., Wash., D.C.
9. **Agency Contact:** Dr. C. David Wise, NIAID, Bldg. 31, Rm. 7A-19, NIH Bethesda, MD 20205
10. **Cost:** FY 82 - $150, FY 83 - $150, FY 84 - $181
11. **Fund Source:** Evaluation 12. **Mechanism:** Contract
13. **Project No.:** NIAID 82-301 14. **Contract No.:** NOI-AI-22678
15. **NTIS NO.:** X-NYD 16. **ERIC No.:** NA
17. **Program(s) Evaluated:** PHS-NIH-Biomedical Research-Institute Specific-Allergy and Infectious Diseases Accelerated Development of New Vaccines Program
18. **Evaluation Type:** Program Strategy
19. **Descriptors:** Communicable Disease, Preventive Health Care
20. **Abstract:** The Institute of Medicine (IOM) convened a group of experts to develop a model for setting priorities among vaccines for diseases of importance to the general U.S. population. IOM obtained and used relevant data so as to quantify the various components of the decision making aspects of the model e.g., epidemiological data, mortality and morbidity data, cost of illness, scientific readiness, incidence and prevalence of target diseases, cost effectiveness, patient and physician acceptance, safety and efficacy etc. Using the model, IOM evaluated five vaccines--that IOM and the NIAID Steering Group had agreed were ready scientifically for accelerated development--and provided NIAID with a list of these candidate vaccines in order of priority. In a second phase of the study, IOM will consider candidate vaccines for diseases of importance to less technologically advanced nations, and develop a model for setting priorities among vaccines whose development could be accelerated.

10

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Dr. Duane Alexander, Acting Director

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List of Projects and Proposed Budget 10.3

Previously Approved Projects Deferred to FY 1986 10.5

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National Institute of Child Health and Human Development: Proposed Budget

		$ in Thousands FY 85	 FY 86	 FY 87
NICHD 84-401	Evaluation of Contraceptive Development Program	(2)	--	--
NICHD 84-402	Evaluation of Contraceptive Evaluation Program	(1)	--	--
NICHD 84-405	Evaluation of Addition of Interviews to the Peer Review of Physician Scientist and Clinical Investigator Applications	(5)	(10)	--
NICHD 85-401	Impact Evaluation of Cesarean Childbirth Consensus Conference	(34)	--	--
NICHD 85-402	Update of NICHD Congenital Defects Program Research Plan	--	(22)	--
NICHD 85-403**	Update of NICHD Nutrition Program Research Plan	--	--	(22)
NICHD 85-404*	Update of NICHD Pregnancy, Birth, & the Infant Program Research Plan	--	(25)	--
NICHD 85-405**	Update of NICHD Fertility and Infertility Program Research Plan	--	--	(22)
NICHD 85-406*	Update of NICHD Demographic and Behavioral Sciences Program Research Plan	--	(22)	--
NICHD 86-401	Impact Evaluation of Grants Process Orientation for Pediatric Scientist Training Program	--	(5)	--
Total FY 86 NICHD Evaluation Fund Request			($84)	

Notes

( ) - non set-aside funds
* - approved for FY 85, deferred to FY 86
** - approved for FY 85, deferred to FY 87

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NICHD 85-404

2. Project Title and Capsule Description:

   a. Title: Update of NICHD Pregnancy, Birth, and the Infant Program Research Plan

   b. Capsule Description: As a means of setting objectives for the evaluation of this program, this project will update the state-of-the-science assessment and the resultant program goals and objectives developed for the Pregnancy, Birth, and the Infant (PBI) Program as part of the NICHD Research Plan (NICHD 80-305/306). The FY 1984 budget of the PBI Program is estimated to be $30.2 million.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)
86	($25)	--

Note: ( ) denotes NICHD funds

The estimated cost of this project is based on a calculation of the costs of professional services contracts with 10-12 consultants, including the expenses of their attending two meetings in Bethesda plus paying them a small fee for developing a paper. It greatly strengthens the project to use outside expert consultants to perform the update assessment of the state-of-the-science. Based on the outside experts' updated assessment and their own knowledge of the program, Institute program staff will update the program's goals and objectives so that the program can be evaluated.

4. Project Monitor/Contact:

Charlotte S. Catz, M.D., Chief
Pregnancy and Perinatology Section
National Institute of Child Health and Human Development
Room 7C-09
7910 Woodmont Avenue
Bethesda, Maryland 20205
(301) 496-5575

5. Coordination: This project has been reviewed by the NICHD Director, Deputy Director, Director of the Center for Research for Mothers and Children, Chief and Assistant Chief of the Office of Planning and Evaluation, and the Evaluation Officer. No personnel of other agencies will have coordinative responsibility for this project.

6. Program Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; and PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development.

7. Intended Users: The intended users of the information produced by this project include the NICHD Director, Deputy Director, Director of the Center for Research for Mothers and Children, Chief and Assistant Chief of the Office of Planning and Evaluation, as well as the Chief and staff of the Pregnancy and Perinatology Section.

   The project will begin in October of 1985 and conclude in September of 1986. The final report will be provided to the intended users by the first of October 1986.

8. Information to be Generated: In updating the PBI portion of the NICHD Research Plan, this project will obtain the judgments and efforts of outside experts to: 1) develop an updated overview and historical perspective of this area of science; 2) document the field's recent significant findings and achievements; 3) identify current gaps in knowledge; and 4) make timely recommendations for future activities of this program. Using this updated assessment of the state-of-the-science and detailed program information, program and other Institute staff will update the program goals and objectives developed for this program as part of the NICHD Research Plan (NICHD 80-305/306), facilitating an evaluation of the program.

9. Approach: Program staff will select a group of 10-12 outside consultants, who are experts in this area of research, to update the state-of-the-science assessment of this field. Supported by professional services contracts, the consultants, as a group, will meet to discuss the project and accept assignments to develop papers on their areas of particular expertise. In an effort to make their papers representative of their fields, each consultant will obtain the opinions of a group of his or her peers established to guide and review the development of the paper. If needed, the consultants will meet again to review their papers. The program staff, with the assistance of several of the consultants, will blend the papers into a single, updated, state-of-the-science assessment report. This report will be published and will serve as the basis for program and other Institute staff to develop updated program goals and objectives for use in evaluating and managing this program.

10. Information Clearance/Collection: No

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NICHD 85-406

2. Project Title and Capsule Description:

   a. Title: Update of NICHD Demographic and Behavioral Sciences Program Research Plan

   b. Capsule Description: As a means of setting objectives for the evaluation of this program, this project will update the state-of-the-science assessment and the resultant program goals and objectives developed for the Demographic and Behavioral Sciences (DBS) Program as part of the NICHD Research Plan (NICHD 80-305/306). The FY 1984 budget of the DBS Program is estimated to be $14.4 million.

3. Cost and Funding Source:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)
86	($22)	--

Note: ( ) denotes NICHD funds

The estimated cost of this project is based on a calculation of the costs of professional services contracts with 10-12 consultants, including the expenses of their attending two meetings in Bethesda plus paying them a small fee for developing a paper. It greatly strengthens the project to use outside expert consultants to perform the update assessment of the state-of-the-science. Based on the outside experts' updated assessment and their own knowledge of the program, Institute program staff will update the program's goals and objectives so that the program can be evaluated.

4. Project Monitor/Contact:

Wendy Baldwin, Ph.D., Chief
Demographic and Behavioral Sciences Branch
National Institute of Child Health and Human Development
Room 7C-25
7910 Woodmont Avenue
Bethesda, Maryland 20205
(301) 496-1174

5. Coordination: This project has been reviewed by the NICHD Director, Deputy Director, Director of the Center for Population Research, Chief and Assistant Chief of the Office of Planning and Evaluation, and the Evaluation Officer. No personnel of other agencies will have coordinative responsibility for this project.

6. Program Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; and PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development.

Research Grants and Contracts; and PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development.

7. Intended Users: The intended users of the information produced by this project include the NICHD Director, Deputy Director, Director of the Center for Population Research, Chief and Assistant Chief of the Office of Planning and Evaluation, as well as the Chief and staff of the Demographic and Behavioral Sciences Branch.

   The project will begin in October of 1985 and conclude in December of 1986. The final report will be provided to the intended users by the first of January 1987.

8. Information to be Generated: In updating the DBS portion of the NICHD Research Plan, this project will obtain the judgments and efforts of outside experts to: 1) develop an updated overview and historical perspective of this area of science; 2) document the field's recent significant findings and achievements; 3) identify current gaps in knowledge; and 4) make timely recommendations for future activities of this program. Using this updated assessment of the state-of-the-science and detailed program information, program and other Institute staff will update the program goals and objectives developed for this program as part of the NICHD Research Plan (NICHD 80-305/306), facilitating an evaluation of the program.

9. Approach: Program staff will select a group of 10-12 outside consultants, who are experts in this area of research, to update the state-of-the-science assessment of this field. Supported by professional services contracts, the consultants, as a group, will meet to discuss the project and accept assignments to develop papers on their areas of particular expertise. In an effort to make their papers representative of their fields, each consultant will obtain the opinions of a group of his or her peers established to guide and review the development of the paper. If needed, the consultants will meet again to review their papers. The program staff, with the assistance of several of the consultants, will blend the papers into a single, updated, state-of-the-science assessment report. This report will be published and will serve as the basis for program and other Institute staff to develop updated program goals and objectives for use in evaluating and managing this program.

10. Information Clearance/Collection: No

Not Reviewed by
NIH Technical Review Committee

1. Project ID # and Title: NICHD 86-401 Impact Evaluation of Grants Process Orientation for Pediatric Scientist Training Program

2. Information to be Generated: The Institute's Pediatric Scientist Training Program will conduct a grants process orientation for selected personnel from universities with schools of pediatrics to assist them in becoming more familiar with NICHD/NIH research opportunities. This project will obtain the trainees' evaluation of the benefit of this orientation.

3. Intended Use: The Institute would consider additional orientation sessions, perhaps on a regular basis, if it can be determined that they would be beneficial to these institutions and potential grantees.

4. Cost and Timing:

Fiscal Year	Expenditures (in thousands)	DCRT Charges (in thousands)
86	($5)	--

Note: ( ) denotes NICHD funds

The evaluation instrument for the trainees will be developed in the next few months, and the orientation session, where the instrument will be administered, is being planned for November of 1985. An assessment of the evaluation results will be available in January of 1986.

5. OMB Review: No

1. EDC ID No.: 2143 2. Entry Dates: 3. Status: Completed

4. Project Title: Stage 2 Evaluation of NICHD Child and Adolescent Development Research Program

5. Final Report Title: National Institute of Child Health & Human Development, Center for Research for Mothers & Children, Human Learning and Behavior Branch, Five Year Plan

6. Agency Sponsor: PHS-NIH-NICHD 7. Start/End Dates: 82-09, 84-12

8. Performer: Professional Services Consultants

9. Agency Contact: George W. Gaines, NICHD
Bldg. 31, Rm. 2A-16
Bethesda, MD 20892
(301) 496-1877

10. Cost: FY83-$17 ,FY84-$3 ,FY85-$0 ,FY -$,FY -$

11. Fund Source: Evaluation 12. Mechanism: Professional Services Contracts

13. Project No.: NICHD 82-302 14. Contract/Grant No.: NA

15. NTIS No.: NA 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; PHS-NIH-Biomedical Research-Institute Specific-Child Health and Human Development

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research; Children and Youth; Family; Grant and Contract Management; Management Information and Reporting; Maternal and Child Health; Research and Evaluation Feature; Research and Evaluation Planning and Administration

20. Abstract: As a means of setting objectives for the evaluation of this program, this project updated the state-of-the-science assessment and the resultant program goals and objectives developed for this program as part of the NICHD Research Plan (NICHD 80-305/306). Seventeen expert consultants, with the guidance of an additional 151 expert consultants, produced papers which 1) developed an updated overview and historical perspective of this area of science; 2) documented the field's recent significant findings and achievements; 3) identified current gaps in knowledge; and 4) made timely recommendations for future activities of this program. Program staff consolidated the papers into five chapters, which were edited and then reviewed by NICHD staff and the NICHD National Advisory Council. The final report developed program goals, objectives, and specific action steps for this research program.

1. EDC ID No.: 2143.1 2. Entry Dates: 3. Status: Ongoing

4. Project Title: Stage 2 Evaluation of NICHD Mental Retardation Research Program

5. Final Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NICHD

7. Start/End Dates: 82-09, 86-03

8. Performer: Expert Consultants

9. Agency Contact: George W. Gaines, NICHD
Bldg. 31, Rm. 2A-16
Bethesda, MD 20892
(301) 496-1877

10. Cost: FY83-($0) ,FY84-($0) ,FY85-($0) ,FY86-($0) ,FY -$

11. Fund Source: No Cost

12. Mechanism: In House

13. Project No.: NICHD 82-304

14. Contract/Grant No.: NA

15. NTIS No.: NA

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; PHS-NIH-Biomedical Research-Institute Specific-Child Health and Human Development

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research; Children & Youth; Family; Grant & Contract Management; Management Information & Reporting; Maternal & Child Health; Research & Evaluation Feature; Research & Evaluation Planning & Administration

20. Abstract: As a means of setting objectives for the evaluation of this program, this project is updating the state-of-the-science assessment and the resultant program goals and objectives developed for this program as part of the NICHD Research Plan (NICHD 80-305/306). Sixteen expert consultants, with the guidance of several professional organizations and numerous additional consultants, have produced papers which 1) develop an updated overview and historical perspective of this area of science; 2) document the field's recent significant findings and achievements; 3) identify current gaps in knowledge; and 4) make timely recommendations for future activities of this program. Program staff are "crosswalking" and consolidating the papers, and will have a draft document for internal review in November and Council review in January. The final document will be completed before the end of March.

1. EDC ID No.: X-NYD 2. Entry Dates: 3. Status: Ongoing

4. Project Title: Evaluation of Contraceptive Development Program

5. Final Report Title: NYD

6. Agency Sponsor: PHS-NIH-NICHD

7. Start/End Dates: 84-01, 85-12

8. Performer: Professional Services Consultants

9. Agency Contact: Gaines, George W.
Bldg. 31, Rm. 2A-16
(301)496-1877

10. Cost: FY84-($4) ,FY85-($2) ,FY -$,FY -$,FY -$

11. Fund Source: NICHD

12. Mechanism: Professional Services Contracts

13. Project No.: NICHD 84-401

14. Contract/Grant No.: NA

15. NTIS No.: NA

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; and PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Biomedical Research, Family Planning, Federal Administration, Grant and Contract Management, Research and Evaluation Performance, Research and Evaluation Planning and Administration

20. Abstract:
This is a full-scale program performance evaluation to assess the progress, effectiveness, and efficiency of the Contraceptive Development Program in meeting its research goals and objectives. The study is the responsibility of a committee of six outside expert consultants. The committee has met twice and several subcommittee meetings have been held. Decisions on the conclusion of this project are to be made in the near future.

1. EDC ID No.: 2373 2. Entry Dates: 3. Status: Ongoing

4. Project Title: Evaluation of Contraceptive Evaluation Program

5. Final Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NICHD 7. Start/End Dates: 84-01, 85-12

8. Performer: Professional Services Consultants

9. Agency Contact: Gaines, George W.
Bldg. 31, Rm. 2A-16
(301)496-1877

10. Cost: FY84-($1) ,FY85-($1) ,FY -$,FY -$,FY -$

11. Fund Source: NICHD 12. Mechanism: Professional Services Contracts

13. Project No.: NICHD 84-402 14. Contract/Grant No.: NA

15. NTIS No.: NA 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; and PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Biomedical Research; Family Planning; Federal Administration; Grant and Contract Management; Research and Evaluation Performance; Research and Evaluation Planning and Administration

20. Abstract:

This is a full-scale program performance evaluation to assess the progress, effectiveness, and efficiency of the Contraceptive Evaluation Program in meeting its research goals and objectives. The study is the responsibility of a committee of six outside expert consultants. The committee has met twice and several subcommittee meetings have been held. Decisions on the conclusion of this project are to be made in the near future.

1. EDC ID No.: 2375 2. Entry Dates: 3. Status: Completed

4. Project Title: Update of NICHD Physiological Development and Endocrinology Research Plan

5. Final Report Title: Child Health & Human Development: An Evaluation & Assessment of the State of the Science, Report of the Study Group on Developmental Endocrinology and Physical Growth. Child Health & Human Development: Five Year Plan, Report on Developmental Endocrinology & Physical Growth

6. Agency Sponsor: PHS-NIH-NICHD

7. Start/End Dates: 84/04, 85/06

8. Performer: Professional Services Consultants

9. Agency Contact: George W. Gaines, NICHD
Bldg. 31, Rm. 2A-16
Bethesda, MD 20892
(301) 496-1877

10. Cost: FY84-($22) ,FY85-($0) ,FY -$,FY -$,FY -$

11. Fund Source: NICHD

12. Mechanism: Professional Services Contracts

13. Project No.: NICHD 84-404

14. Contract/Grant No.: NA

15. NTIS No.: NA

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; PHS-NIH-Biomedical Research-Institute Specific-Child Health and Human Development

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research; Children & Youth; Family; Grant & Contract Management; Management Information & Reporting; Maternal & Child Health; Research & Evaluation Feature; Research & Evaluation Planning & Administration

20. Abstract: As a means of setting objectives for the evaluation of this program, this project updated the state-of-the-science assessment and the resultant program goals and objectives developed for this program as part of the NICHD Research Plan (NICHD 80-305/306). Thirty-one expert consultants, divided into seven workgroups, developed papers which summarize 1) the state of the science in each of the seven areas, 2) the promising areas for future research, and 3) specific recommendations for program emphases in the near (1-2 year) and long (3-5 year) term. The final draft documents were reviewed by NICHD staff and the NICHD National Advisory Council.

1. EDC ID No.: X-NYD 2. Entry Dates: 3. Status: Ongoing

4. Project Title: Evaluation of Addition of Interviews to the Peer Review of Physician Scientist and Clinical Investigator Applications

5. Final Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NICHD

7. Start/End Dates: 84-07, 86-02

8. Performer: In House

9. Agency Contact: Slater, Stanley L.
Rm. 6C-08 Landow Bldg.
(301)496-1696

10. Cost: FY84-($2) ,FY85-($5) ,FY86-$(10) ,FY -$,FY -$

11. Fund Source: NICHD

12. Mechanism: In House

13. Project No.: NICHD 84-405

14. Contract/Grant No.: NA

15. NTIS No. NA

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Research Grants and Contracts; and PHS-NIH-Biomedical Research-Institute Specific-Child Health and Human Development

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research; Federal Administration; Grant and Contract Management; Scientific Manpower

20. Abstract:
This project is seeking to answer the question of whether the addition of an interview will benefit the peer review of Physician Scientist (K11) and Clinical Investigator (K08) career development grant applications. Specifically, the study is evaluating whether the addition of interviews will provide reviewers with information that assists them in their selection of candidates. The study interview and scoring procedures developed for this project were used during the March and June 1985 review rounds, and will be used at the December and, possibly, January 1986 review rounds. The NICHD Biometry Branch is performing a statistical analysis of the data being collected during the reviews. A final report will be prepared in February 1986.

1. EDC ID No.: X-NYD 2. Entry Dates: 3. Status: Ongoing

4. Project Title: Impact Evaluation of Cesarean Childbirth Consensus Conference

5. Final Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NICHD 7. Start/End Dates: 84-10, 86-02

8. Performer: ACOG
600 Maryland Ave., S.W.
Washington, D.C. 20024-2588

9. Agency Contact: Berendes, Heinz W.
Rm. 8B-06 Landow Bldg.
(301)496-5064

10. Cost: FY85-($34) ,FY -$,FY -$,FY -$

11. Fund Source: NICHD 12. Mechanism: Contract

13. Project No.: NICHD 85-401 14. Contract/Grant No.: NYD

15. NTIS No.: NA 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development

18. Evaluation Type: Program Impact

19. Descriptors: Biomedical Research; Federal Administration; Research and Evaluation Planning and Administration

20. Abstract:
The study is seeking the answers to the following two questions: 1) What changes occurred in the Cesarean Childbirth practices of American medicine during the period 1980 to 1983? and 2) What role did the 1980 Cesarean Childbirth Consensus Conference play in affecting those changes? The American College of Obstetricians and Gynecologists has conducted a survey of the Cesarean Childbirth policies and practices of a sample of American hospitals and obstetricians. The NICHD has obtained this data and is in the process of analyzing it.

1. EDC ID No.: X-NYD 2. Entry Dates: 3. Status: Ongoing

4. Project Title: Update of NICHD Congenital Defects Program Research Plan

5. Final Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NICHD

7. Start/End Dates: 84-10, 86-06

8. Performer: Professional Services Contracts

9. Agency Contact: Dayton, Delbert H.
Rm. 7C-09 Landow Bldg.
(301)496-5575

10. Cost: FY85-($0) ,FY86-$(22) ,FY -$,FY -$,FY -$

11. Fund Source: NICHD

12. Mechanism: Professional Services Contracts

13. Project No.: NICHD 85-402

14. Contract/Grant No.: NA

15. NTIS No.: NA

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH-Biomedical Research-Activity-Institute Specific-Child Health and Human Development

18. Evaluation Type: Program Performance Evaluation

19. Descriptors: Biomedical Research; Federal Administration; Maternal and Child Health, Research and Evaluation Planning and Administration

20. Abstract:
As a means of setting objectives for the evaluation of this program, this project is updating the state-of-the-science assessment and the resultant program goals and objectives developed for this program as part of the NICHD Research Plan (NICHD 80-305/306). The final report of this project will be reviewed by NICHD staff and the NICHD National Advisory Council.

11

NATIONAL INSTITUTE OF DENTAL RESEARCH

Dr. Harald Löe, Director

Contents

List of Projects and Proposed Budget 11.3

Evaluation Documentation Center Forms for Continuing and Recently Completed Projects 11.5

National Institute of Dental Research: Proposed Budget:

		$ in Thousands FY 85	FY 86	FY 87
NIDR 83-301	Evaluation of Selected Oral Health Education and Promotion Activities of the National Caries Program	---	---	---
NIDR 83-302	Assessment of the Effectiveness of NIDR Training Programs in Preparing Dental Clinical Investigators	---	---	---
NIDR 85-401	NIDR Long-Range Research Plan: Creation of a Database and a Monitoring/Implementation Process	(10)	---	---
Total FY 86 NIDR Evaluation Fund Request			($0)	

NOTE:
( ) denotes Non NIH Set-Aside Funds

1. **EDC ID No.** 2138 **Project No.:** NIDR 83-301

2 **Entry Dates:** 3. **Status:** In Process

4. **Project Title:** Evaluation of Selected Oral Health Education and Promotion Activities of the National Caries Program

5. **Report Title:** NYD

6. **Agency Sponsor:** PHS-NIH-NIDR 7. **Start/End Dates:** 83-09, 86-01

8. **Performer:** Health Inquiry, Inc.
4832 Elliott Avenue
Minneapolis, Minnesota 55417
Telephone: (612) 824-3469

9. **Agency Contact:** Kleinman Dr. Dushanka V.; Bldg 31, Rm 2C-36; NIDR, NIH
(301) 496-6705

10. **Cost:** FY 83-$90, FY 84-$3

11. **Fund Source:** Evaluation 12. **Mechanism:** Contract

13. **Project No.:** NIDR 83-301 14. **Contract No:** NO 1-DE-1-32445

15. **NTIS No.** NYD 16. **ERIC No:** NA

17. **Program(s) Evaluated:** PHS NIH Biomedical Research Institute Specific-Dental

18. **Evaluation Type:** Program Management

19. **Descriptors:** Survey or Questionnaire Feature, Educational Techniques, Dental Manpower

20. **Abstract:** The purpose of the project is to determine the need for improved education and promotion activities of caries preventive procedures and techniques directed towards educators of dental hygiene students. For this determination, educators directly involved in the teaching of caries preventive measures in all 201 U.S. dental hygiene schools will be surveyed. They will be asked about the teaching of related topics and their needs for future information and materials regarding these topics. The results of the study will be disseminated through an agency report and journal articles.

1. EDC ID No. 2376 Project No.: NIDR 83-302

2 Entry Dates: 3. Status: In Process

4. Project Title: Assessment of the Effectiveness of NIDR Training Programs in Preparing Dental Clinical Investigators

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIDR 7. Start/End Dates: 83/06, 85-12

8. Performer: Computer Horizons, Inc.
1050 Kings Highway North
Cherry Hill, New Jersey 08034

9. Agency Contact: Brown Dr. L. Jackson; Bldg 31, Rm 2C-36; NIDR, NIH (301) 496-6705

10. Cost: FY 84-$48

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NIDR 83-302 14. Contract No: N01-OD-1-2109

15. NTIS No. NYD 16. ERIC No: NA

17. Program(s) Evaluated: NIDR Extramural Program; NRSA Post-Doctoral Research Training Grants and Fellowship Program

18. Evaluation Type: Program Impact

19. Descriptors: NIDR Training Programs: NRSA Post-doctoral Research Training Grants and Fellowships
Dental Manpower

20. Abstract: This project is studying the adequacy of the supply of dental clinical investigators, their educational preparation, and subsequent commitment to productive careers in clinical research. Using available secondary data, the effectiveness of NIDR programs used to train clinical investigators is being evaluated and the need for such researchers, in both quantitative and qualitative terms, determined. Based on an assessment of past programs' accomplishments and deficiencies, plus an analysis of factors in the dental educational system associated with research training, recommendations for improving the NIDR training program will be made. The results of the study will be disseminated through journal articles.

1. EDC ID No. Project No.: NIDR 85-401

2 Entry Dates: 3. Status: In Process

4. Project Title: NIDR Long-Range Research Plan: Creation of a Database and a Monitoring/Implementation Process

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIDR 7. Start/End Dates: 84/07, 85-12

8. Performer: In-house

9. Agency Contact: Kleinman, Dr. Dushanka, Bldg 31, Rm 2C-36, NIDR, NIH (301) 496-6705

10. Cost: FY 85-($10)

11. Fund Source: Evaluation 12. Mechanism: In-house, Purchase Order

13. Project No.: NIDR 85-401 14. Contract No: NA

15. NTIS No. NYD 16. ERIC No: NA

17. Program(s) Evaluated: NIDR Extramural Program

18. Evaluation Type: Program Impact

19. Descriptors: NIDR Extramural Programs

20. Abstract: This project will establish a database and develop a monitoring/implementation process for the NIDR Long-Range Research Plan. The database will entail coding all applications and awards according to the research objectives and strategies presented in the Plan. The monitoring/implementation process will describe the formation and use of the database for Institute management needs. Such a system should facilitate the management of extramural and intramural research programs as they relate to the Plan. The Plan, targeted for FY 1985-89, has 168 research objectives and 55 strategies which represent a total of 14 areas of investigation. The results of the study will be disseminated through agency reports.

12.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Dr. David P. Rall, Director

Contents

List of Projects and Proposed Budget 12.3

Evaluation Documentation Center Forms for Continuing and Recently Completed Projects 12.5

National Institute of Environmental Health Sciences: Proposed Budget

		$ in Thousands		
		FY 85	FY 86	FY 87
NIEHS 83-401	Manpower in the Field of Environmental Epidemiology: Evaluation and Survey	-- (165)	-- (--)	-- (--)
NIEHS 84-401	Third Task Force on Research Planning in Environmental Health Science	-- (70)	-- (--)	-- (--)
NIEHS 84-402	Panel on Chemical Carcinogenesis Testing and Evaluation	-- (--)	-- (--)	-- (--)
NIEHS 84-403	Manpower in the Field of Environmental Toxicology: Evaluation and Survey	-- (185)	-- (--)	-- (--)
NIEHS 84-404	NIEHS Program Analysis System	-- (--)	-- (292)	-- (270)
	Total FY 86 NIEHS Evaluation Fund Request		(292)	

Notes

( ) - non set-aside funds

Project No.: NIEHS 83-401

1. EDC ID No.: 2535

2. Entry Dates:

3. Status: In Process

4. Project Title: Manpower in the Field of Environmental Epidemiology - Evaluation and Survey

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIEHS

7. Start/End Dates: 84-09, 87-03

8. Performer: CSR, Incorporated
805 15th Street, Suite 500
Washington, D.C. 20005

9. Agency Contact: Dr. Christopher O. Schonwalder
P.O. Box 12233
Research Triangle Park, N.C. 27709
FTS 629-7634 or (919) 541-7634

10. Cost: FY 84-($76), FY 85-($165)

11. Fund Source: In-House

12. Mechanism: Contract

13. Project No : NIEHS 83-401

14. Contract No.: NO1-ES-4-5049

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Activity-Training

18. Evaluation Type: Program Impact

19. Descriptors: Environmental Health, Health Manpower Training, Health Manpower Projections, Survey or Questionnaire Feature, Statistical Data Feature, Federal Administration

20. Abstract: This evaluation project is intended to analyze the current environmental epidemiology supply and demand, project future supply and demand for environmental epidemiologists, and determine the contribution of NIEHS' training support to the overall training effort in the field. NIEHS plans to determine the number of environmental epidemiologists trained in the United States and describe the nature of their training; enumerate existing training programs in environmental epidemiology and describe and classify the major components of such training programs; obtain statistics and estimates of current and future (five-year) outputs of training programs in environmental epidemiology; and analyze five-year employment histories of past trainees in environmental

epidemiology to 1) determine if oversupply or demand exists and 2) ascertain if trainees are employed in the fields specified in their training. The latter objective can elucidate the role played by NIEHS in stimulating the development of the environmental field. NIEHS also plans to determine the current and future (five-year) demand for environmental epidemiologists in academic, industrial, and governmental sectors of the economy. This study will help NIEHS meet the challenge of producing the sound estimates of manpower supply and demand in environmental epidemiology that are necessary for planning and budgeting purposes. It also will formulate recommendations regarding future training and program development in the field. For the survey, environmental epidemiology is defined as the study of the relationship of environmental factors to the occurrence of mental and physical disease including adverse reproductive outcome in human populations. The determinants of primary concern are chemical and physical extrinsic agents to which humans are exposed; other determinants of disease which might influence exposure, susceptibility, or response to extrinsic agents include host factors (e.g., age, sex) and physical, biologic, and socioeconomic factors (e.g., climate, population density, urbanization). The final agency report will be distributed widely.

Project No.: NIEHS 84-401

1. EDC ID No.: 2377

2. Entry Dates:

3. Status: In Process

4. Project Title: Third Task Force on Research Planning in Environmental Health Science

5. Report Title: Human Health and the Environment - Some Research Needs: Report of the Third Task Force for Research Planning in Environmental Health Science

6. Agency Sponsor: PHS-NIH-NIEHS

7. Start/End Dates: 83/09, 85/06

8. Performer: New York University Medical Center
550 First Avenue
New York, New York 10016

9. Agency Contact: George M. Kingman
P.O. Box 12233
Research Triangle Park, N.C. 27709
FTS 629-3484 or (919) 541-3484

10. Cost: FY 83-($432), FY 84-($0), FY 85-($70)

11. Fund Source: Grants

12. Mechanism: Cooperative Agreement

13. Project No.: NIEHS 84-401

14. Contract No.: NA

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Environmental Health

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research, Environmental Health, Federal Role, Needs and Needs Assessment, Research and Evaluation Planning and Administration

20. Abstract: The National Advisory Environmental Health Sciences Council (NAEHSC), at the direction of the House Committee on Appropriations, and through the Third Task Force on Research Planning in Environmental Health Science (Task Force III), assessed the state of existing knowledge and identified areas of particular scientific opportunity so that NIEHS will have clearly defined direction and priorities over the next seven to eight years. The report of the Task Force is the product of the

scientific community at large, reflecting that group's best judgement about areas exceptionally worthy of pursuit, which the Congress may use as a touchstone in setting appropriate funding levels for the Institute. It was submitted to the Committee on Appropriations in January 1985. The Task Force III report concentrates primarily on those areas of research promise in which scientific advances can be expected to have the greatest impact in preventing or alleviating the environmental health problems of the coming decades. The five broad topic areas addressed are: 1) biological mechanisms through which physical and chemical agents give rise to disease, 2) methods for assessing the health significance of exposure to toxic agents, 3) research strategies for preventing environmentally provoked diseases, 4) organization and structure of environmental health research in the U.S., and 5) information exchange in the environmental health sciences. In addressing each of these topic areas and their ramifications, the report considers such questions as the current state of the relevant knowledge (including cogent epidemiological investigations and data bases), key research needs, promising research opportunities, and impediments to research progress. The scope of this report is exceedingly broad, ranging from studies at the subcellular and molecular levels to institutional relationships affecting large human population groups and complex organizations. To this extent, the recommendations presented are directed not only to scientists, but also to concerned persons of many disciplines. For this reason, the Institute will distribute the report widely when the printed copies become available in the fall of 1985.

Project No.: NIEHS 84-402

1. EDC ID No: 2379

2. Entry Dates

3. Status: Complete

4. Project Title: Panel on Chemical Carcinogenesis Testing and Evaluation

5. Report Title: Report of the NTP Ad Hoc Panel on Chemical Carcinogenesis Testing and Evaluation

6. Agency Sponsor: PHS-NIH-NIEHS

7. Start/End Dates: 83/05, 84/08

8. Performer: Panel Commissioned by the National Toxicology Program (NTP) Board of Scientific Counselors

9. Agency Contact: Dr. David P. Rall
P.O. Box 12233
Research Triangle Park, N.C. 27709
FTS 629-3201 or (919) 541-3201

10. Cost: FY 83-$50, FY 84-$80

11. Fund Source: In-House

12. Mechanism: Professional Services Contract

13. Project No.: NIEHS 84-402

14. Contract No.: NA

15. NTIS No.: EDC Only

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research, Environmental Health, Federal Role, Needs and Needs Assessment, Research and Evaluation Planning and Administration

20. Abstract: The Ad Hoc Panel on Chemical Carcinogenesis Testing and Evaluation was established in response to a recommendation from the March 1983 meeting of the National Toxicology Program (NTP) Board of Scientific Counselors. The charge to the Panel was to review the basic biology and chemistry of carcinogenesis and to recommend to the Board of Scientific Counselors methods NTP should use for detecting and evaluating chemical carcinogens. The Panel surveyed the state-of-the-art reflecting advances made since the last thorough published evaluation of chemical carcinogenesis testing by the National Cancer Institute in the 1970s. The establishment in 1978 of NTP led to broadening the objectives of the

testing and, therefore, changing long-term testing procedures. The Panel was convened to review current testing procedures in light of newer scientific information. Its recommendations to the Board are aimed at ensuring that NTP methodology for assessing chemical carcinogenesis remains in the forefront. To evaluate current knowledge in the area of carcinogenesis testing and make recommendations that meet the scientific and regulatory needs in this area, the Panel was divided into four subpanels to deal with the general areas of short-term tests, subchronic studies and related issues, chronic studies, and regulatory aspects. The conclusions of the Panel are stated as a series of recommendations to the Board of Scientific Counselors. These deal with practical aspects of the bioassay, as well as possible future studies extending methodology and resolving persistent questions. In reviewing the bioassay and related studies, the Panel found: 1) the ongoing NTP effort has benefited from the existing peer review process and is continuing to evolve scientifically, 2) the issue of quality assurance is gaining appropriate recognition, and 3) many of the Panel's recommendations were, in fact, anticipated by NTP managers. The report of the Panel is being distributed widely; copies are available from the NTP Public Information Office.

Project No.: NIEHS 84-403

1. EDC ID No.: 2533

2. Entry Dates:

3. Status: In Process

4. Project Title: Manpower in the Field of Environmental Toxicology - Evaluation and Survey

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIEHS

7. Start/End Dates: 84-09, 87-03

8. Performer: Research Triangle Institute (RTI)
P.O. Box 12194
Research Triangle Park, N.C. 27709

9. Agency Contact: Dr. Christopher O. Schonwalder
P.O. Box 12233
Research Triangle Park, N.C. 27709
FTS 629-7634 or (919) 541-7634

10. Cost: FY 84-($66), FY 85-($185)

11. Fund Source: In-House

12. Mechanism: Contract

13. Project No.: NIEHS 84-403

14. Contract No.: NO1-ES-4-5074

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Activity-Training

18. Evaluation Type: Program Impact

19. Descriptors: Environmental Health, Health Manpower Training, Health Manpower Projections, Survey or Questionnaire Feature, Statistical Data Feature, Federal Administration

20. Abstract: This evaluation project is designed to assess the degree to which the production of environmental toxicologists (both numbers and types) meets the marketplace demand for these professionals. Further, the impact of NIEHS training support on the environmental toxicology training effort will be analyzed. To realize these purposes, the study will describe the nature of current environmental toxicology academic and training programs (e.g., curricula, faculty, and student characteristics, program emphasis); design an information system for monitoring the match between toxicology training programs and employment needs in industry, government, and academia through a plan for annually updating

survey information; and communicate the results of the research effort through 1) holding a conference/workshop on training in environmental toxicology and 2) disseminating the final report and conference proceedings widely. The study will describe current government programs providing support for training of environmental toxicologists; and identify differences among academic/training programs that may relate to differential impact upon the marketplace for program graduates. NIEHS also plans to assess employers' current and projected needs for differing numbers and types (specialties and subspecialties) of environmental toxicology professionals; conduct a supply and demand analysis from collected data; and describe perceptions of professional society placement bureaus and services regarding the number of graduates and types of training both being provided and requested. Finally, it plans to assess former trainee career progression (e.g., job placement, further education, advancement, responsibility level, career plans, etc.). For the survey, environmental toxicology is defined as the study of environmental chemicals and physical agents, such as noise and radiation, with application of the results to either or both of the following: 1) the prediction, detection, and assessment of environmentally induced human diseases and/or adverse effects; and 2) the development of new knowledge regarding the induction of such diseases and/or adverse effects. This study will assist the Institute in planning and budgeting for its environmental toxicology training program.

Project No.: NIEHS 84-404

1. EDC ID No.: 2378

2. Entry Dates:

3. Status: In Process

4. Project Title: NIEHS Program Analysis System

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIEHS

7. Start/End Dates: 84/04, 89/12

8. Performer: GSA/Computer Sciences Corporation
P.O. Box 12767
Research Triangle Park, N.C. 27709

9. Agency Contact: Jim R. Washington
P.O. Box 12233
Research Triangle Park, N.C. 27709
FTS 629-4497 or (919) 541-4497

10. Cost: FY 84-($50), FY 85-($0), FY 86-($292), FY 87-($270)

11. Fund Source: In-House

12. Mechanism: Interagency Agreement

13. Project No.: NIEHS 84-404

14. Contract No.: NA

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Institute Specific-Environmental Health

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research, Environmental Health, Information Processing, Information Systems, Management Information and Reporting

20. Abstract: This project involves design and development of a program analysis system (PAS) capable of interrelating data on the scientific content of the NIEHS program. This system will meet Institute needs for information to guide priority setting, program management, and planning and evaluation processes. Questions to be dealt with during the course of developing the PAS system include: 1) what are the scope and limitations of data systems already in use and serving some NIEHS needs, 2) what are NIEHS' needs for information and reports, and 3) what data and analytic capabilities must be built into the system to permit future evaluations of Institute activities. In addition to providing the means to consistently

describe NIEHS research activities, the information system will be used to identify trends and gaps in research and to conduct program planning and budgetary analysis. A contract systems analyst already has reviewed all analysis and production work accomplished by various analysts previously; reanalyzed all the more important issues of Institute need for a system; created a general, concept-level design of what the system should be; and outlined steps to be taken to restaff the project and conduct the development process. A government systems analyst currently is being recruited to restart the system development effort which ceased with the loss of the contract analyst. This has resulted in the project being put on hold since August 1984; and it most likely will not be resumed until October 1985 due to the length of time required for recruitment. Once system development is restarted, it is expected that the system will be developed on the inhouse VAX computer. All available database and query packages that operate on the VAX have been critically reviewed and ranked in order of effectiveness, cost, and other pertinent factors. The system must be thesaurus based (which requires the services of an expert) if it is to serve the established Institute needs. This approach, in turn, indicates the need for an Institute central staff of science-knowledgeable personnel to index information into the system; the same staff will handle most inquiries of the system, or at least the most complex ones.

13

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Dr. Ruth L. Kirschstein, Director

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National Institute of General Medical Sciences: Proposed Budget

		$ in Thousands FY 85	 FY 86	 FY 87
NIGMS-82-401	Evaluation of Shared Instrumentation Initiative	--	--	--
NIGMS-86-401	Evaluation of GenBank®--The Genetic Sequence Data Bank	--	($20)	($10)
	Total FY 86 NIGMS Evaluation Fund Request		($20)	

Notes:

( ) non set-aside funds

1. Project ID # and Agency Proposing: NIGMS-86-401

2. Project Title:

   a. Evaluation of GenBank®--The Genetic Sequence Data Bank

   b. The purpose of this evaluation project is to see if this resource is fulfilling the goals of the original contract which are to collect, verify, and annotate the sequences of nucleic acids used by researchers in the molecular biology community to facilitate their basic research. And, based on the need for continued responsiveness to this community, to review the necessity and feasibility of a renewal of the ongoing contract.

3. Cost and Funding source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
FY 86	($20)	--	($20)
FY 87	($10)	--	($10)
FY 88	--	--	--

Note: ( ) denotes BID funds.

Cost Justification: This will be a program performance evaluation. The costs are for in-house administrative and support staff time, and to assume the financial burden of bringing together a group of experts for a one-day review of the GenBank®.

4. Project Monitor/Contact: Christine Carrico, PhD., Director, Pharmacological Sciences Program, National Institute of General Medical Sciences, Westwood Building, Room 919, Bethesda, Maryland 20205, (301) 496-7707

5. Coordination: This proposed study has been reviewed by the Institute Director, Deputy Director, and Institute Scientific Directorate. In addition, senior staff periodically review its progress.

6. Program Evaluated: PHS-NIH-Biomedical Research-Activity-Program Direction and Management; PHS-NIH Biomedical Research-Institute Specific-General Medical Sciences; PHS-NIH-Biomedical Research-Research Resource

The GenBank® is a genetic sequence data bank sponsored by the U.S. Government and available internationally. The current annual budget is about $717,000. It is a collection of all reported nucleic acid sequences, catalogued and annotated for sites of biological significance. It contains information about software that can be used by manipulating sequence data. As new sequences are reported and as new software becomes available, this information is entered into the central GenBank® computer system, maintained by Bolt Beranek and Newman Inc. in Cambridge, Massachusetts.

The database serves scientists around the globe in all research environments. For a nominal fee the database is available to the public in the form of frequently updated computer-readable magnetic tapes and floppy diskettes or as an annual printed compendium. Direct dialup or Telenet on-line access to the central GenBank® computer is available to anyone.

The DataBank was created in 1982 by the National Institute of General Medical Sciences of the National Institutes of Health in response to a critical scientific need. New techniques for analyzing nucleic acids (DNA and RNA) have led to a virtual explosion of data concerning the structure of these molecules. At present there are about 4,000 nucleic acid sequences comprised of approximately 4.3 million nucleotides--and this number is expected to grow at an increasingly rapid rate. This important resource allows researchers, many of them NIH grantees and intramural scientists, to compare similarities between the sequences of different genes without having to go to the literature and perform manual time-consuming searches of articles in various scientific journals. In addition, it allows the examination of the role of mutation in disease states, and ultimately the understanding of how certain genes may have evolved.

7. Intended User: This study is intended to assist program officials, managers, and senior staff who must balance the planning of future expenditures and funds available with the encouragement and support of biomedical research and selected scientific resources.

8. Information to be Generated: The evaluation is intended to meet the information needs of the program managers and policy-makers responsible for the program being evaluated in order to improve the efficiency/effectiveness of that program. The results of a review of the genetic sequence data bank will be used to assess the success of a major activity of the Institute. The information will be used to determine: (1) whether the data bank has been an effective resource in molecular biology research; (2) whether the data bank is serving the scientific community for which it was intended; (3) which aspects of the current project should be retained, expanded, or deleted; and (4) what elements, if any, should be added to the workscope of the new contract to make the database maximally useful, responsive, and cost-effective to its users during the next competitive segment. Further, this evaluation is aimed at determining the need for such a resource, thus providing a foundation for major program decisions about whether it should be renewed and if so, at what level of funding.

9. Approach: The objective of this evaluation will be to assess the success of the GenBank® in fulfilling the goals of the original contract. The original and on-going purpose for this genetic sequence data bank is to collect, verify, and annotate the genetic sequences of nucleic acids. This gathered data are then entered into a computer for rapid retrieval and distribution to interested scientists. It is the Institute's belief that this easy access to the data on nucleic acids (DNA and RNA) will stimulate and facilitate research in molecular biology.

   Even though use of the data bank is high and support for the bank in the scientific community is strong, no evaluation of GenBank®'s actual effectiveness has been performed from the point of view of the basic research it facilitates.

The purpose of this evaluation is to aid us in knowing what the actual contributions the availability of these genetic sequence data in advancing molecular biological research have been. Background information on the GenBank® will be presented to an assembled group of expert molecular biologists, computer specialists, and geneticists at a one-day meeting to be held in Bethesda, Maryland. The information will be evaluated and recommendations regarding the data bank will be utilized by senior staff and program managers in determining whether to prepare an RFP for the renewal of the contract, which terminates on June 30, 1987.

10. Information Clearance/Collection: No

11. Prerulemaking Activity: No

Project No.: NIGMS-82-401

1. EDC ID No.: 2094
2. Entry Dates:
3. Status: In Process

4. Project Title: Evaluation of NIGMS Shared Instrumentation Initiative

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-NIGMS
7. Start/End Dates: 81-09, 86-01

8. Performer: National Institute of General Medical Sciences, NIH, Bethesda, MD 20205
9. Agency Contact: Cassman, Marvin, Westwood Building, Room 903, (301) 496-7463

10. Cost: FY 83-($3), FY 84-($5)

11. Fund Source: S & E
12. Mechanism: In-house

13. Project No.: NIGMS-82-401
14. Contract No.: NA

15. NTIS No.: NYD
16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Institute Specific-General Medical Sciences; PHS-NIH-Biomedical Research Activity-Research Grants and Contracts; PHS-NIH-Biomedical Research Activity-Program Direction and Management

18. Evaluation Type: Research and Data Development

19. Descriptors: Biomedical Research, Grant-in-Aid and Contract Management

20. Abstract: This is a program performance evaluation to determine the success of the NIGMS Shared Instrumentation Program in fulfilling its stated objectives. The program was initiated in FY 1979 to provide grant awards for essential instrument support to groups of investigators having specific needs for such methodologies, and to provide access to those instruments to other researchers who may require it on a more limited scale. Information will be obtained primarily from the progress reports of the principal investigators. The degree of use of the instrument by different research groups will be evaluated through publications referencing use of the tool. In addition, some selected site visits will be made to examine the user logs of the instrument, and to address any problems with those members of the user group listed in the original application.

The outcome of this evaluation should provide information that can be used to determine (1) whether the original goals and objectives have been met, and (2) whether the program should be continued, and at what level.

14

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Dr. Murray Goldstein, Director

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POLICY OVERVIEW: NINCDS EVALUATION STRATEGY

Introduction and Program Structure

The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) is responsible for conducting, sponsoring, and guiding research into the causes, prevention, diagnosis, and treatment of over 650 neurological and communicative disorders. It provides grants-in-aid and contracts to public and private institutions on behalf of individuals who pursue these research interests. The NINCDS also stimulates the recruitment and training of individuals to conduct research in the neurological and communicative fields. It conducts a vigorous and diverse intramural research program at the NIH and in NIH-sponsored clinics and laboratories elsewhere. Finally, the NINCDS actively collects and disseminates information to the general public as well as the biomedical research community.

Because of the number and severity of the disorders NINCDS addresses, the rapidly expanding knowledge base in these areas, and increasingly constrained funding for biomedical research, it is critical that research priorities and strategies be carefully chosen. A wide range of evaluation activities helps NINCDS staff focus and monitor their plans and strategies. These evaluation activities are discussed in this Fiscal Year 1986 Institute evaluation plan.

Role of Evaluation in the NINCDS

Evaluation is implicit in all phases of Institute activity. Evaluation occurs when Institute goals and plans are determined and appraised, when the impacts of the strategies designed to achieve those goals are measured, or when the efficiency or effectiveness of the strategies are judged. Formal and informal evaluation activities assist planning and management and thereby influence the selection of research to be supported by the Institute.

Some evaluations conducted by NINCDS in past years have used Departmental one percent set-aside funds. These projects have been generally separate self-contained projects, and have often been performed under contract. These evaluation projects represent only a small part of the overall evaluation activities NINCDS undertakes. Other activities tend to combine evaluation with planning, management, or budgeting. It is not always easy to separate explicitly the evaluation component from these other functions; they are interrelated.

Evaluation results are actively used in Institute planning and management decisions. The most recent example of a major initiative was the "Evaluation of Research Opportunities and Needs in the Neurological and Communicative Sciences." The results of this study, which was initiated at the direction of the United States Senate Committee on Appropriations, were described in the Fiscal Year 1985 NINCDS Evaluation Plan.

NINCDS Evaluation Framework

A conceptual framework is helpful in highlighting evaluation activities. NINCDS evaluation efforts can be described along two dimensions: (1) by the major Institute function the evaluation supports, and (2) by the participants involved in the evaluation.

A. Institute Function

The major functions of the NINCDS can be summarized as:

- Knowledge development
- Knowledge validation
- Knowledge dissemination and transfer, and
- Institute management

B. Major Participants

The major participants in the NINCDS evaluation process include:

- Advisory Council
- Advisory Committees
- Internal Institute Management

Their respective roles were described in detail in the NINCDS Fiscal Year 1985 Evaluation Plan.

HIGHLIGHTS OF RECENT AND CURRENT EVALUATION EFFORTS

Prominent examples of recent evaluation activities conducted by the NINCDS are described in the following abstracts. Projects are described in two categories: Projects Funded with Evaluation Monies and Activities Funded with Programmatic Monies.

Projects Funded with Evaluation Monies

NINCDS 82-302-Survey of Practice in the Management of Febrile Seizures. The purpose of this study was to determine the frequency with which each physician cares for febrile seizure children, how often they prescribe anticonvulsant medication, and how often they seek consultation. It also determined physicians' rationales for deciding how to treat children who have had febrile seizure(s) and the goals of any treatment. The most preferred medications and contingencies for treatment of side effects were also determined. Questions on current practice in monitoring blood drug levels and hospitalizing the febrile seizure child were included in the survey. Ten thousand physicians in general/family practice, neurology and pediatrics were sent an anonymous questionnaire without any hidden identifiers.

Statistical analyses of the resulting data included cross-classification and tabulations. Recommendations resulting from the study will be made on future directions for febrile seizure research.

NINCDS 83-301-Survey of Antiepileptic Drug Use. The prescribing and dispensing of specific antiepileptic drugs was estimated nationally. The types and frequencies of seizures for which the drugs are prescribed were estimated. This information will provide the NINCDS with information about areas in which new drugs are needed. It will show the impact of drugs recently introduced and provide a baseline reference value against which to measure changes in availability and use of particular antiepileptic drugs in three to five years. Two distinct data collection techniques were utilized: one, a survey of organizations in which drugs are dispensed and prescribed was performed. Organizations included were drug wholesalers, hospitals, and pharmacies; secondly, physicians who treat patients with seizures were also surveyed. Data derived by each technique were linked to provide information on amounts of antiepileptic drugs being used and the number of patients with refractory seizures which persist in spite of available drugs. Study results were disseminated by means of a final contract report.

Activities Funded with Programmatic Monies

While they are seldom funded with evaluation monies, and in fact, are not labeled as official evaluation projects, many management activities conducted by the NINCDS have underlying evaluation components. As the Institute selects its long-term and immediate goals and priorities, identifies emerging problems or opportunities, and assesses its relations with other organizations, it analyzes the productivity, effectiveness and efficiency of its current activities and structures. Frequently this type of evaluation activity may contribute more to the Institute than would a particular formal evaluation project. The types of activities described here are ongoing, intrinsic parts of the Institute planning and management procedures. Recommendations which emerge from each of these activities are seriously considered by the NINCDS and program leadership; the evaluation and its results do not end at the completion of a contract.

Other evaluation activities:

Board of Scientific Counselors. This advisory committee, composed of eight distinguished non-Federal scientists, is responsible for ongoing, comprehensive review of the NINCDS Intramural Research Program (IRP). The Board conducts an indepth analysis of each IRP laboratory and branch on a rotating basis, so that each research unit is evaluated every three to four years. Included in this evaluation is an analysis of the accomplishments of the research unit and individual scientists, alone and in comparison with those of other scientists involved in similar types of research, including an analysis of publications arising from such research. The research accomplishments of the unit, its plan for future research and the resources it will require are thoroughly evaluated by the Board. The recommendations resulting from these reviews are detailed and play a crucial role in the overall management and direction of the Intramural Research Program of the Institute.

NINCDS Implementation Plan. Each year the Director of the NINCDS and the Program Directors and Office Chiefs prepare an Implementation Plan. Developing the Plan requires an evaluation of the previous year's work plan, and is intertwined with all aspects relating to management of the Institute. The Plan articulates underlying objectives, ongoing activities and projects, proposed new activities, budget requirements, accomplishments and problems. The expected contributions of specific activities are stressed, and must be defended. The plan for each organizational component of the Institute is reviewed thoroughly by the Director and key evaluation staff. This review includes all program activities and functions of the Institute and influences its current and future research strategies and goals. During the review process, the plans for the individual units are melded together into a comprehensive plan for the Institute. The finished plan is used throughout the year to coordinate activities of different parts of the Institute, and to serve as a standard for their performance. It also facilitates the preparation of financial information and projections and is a significant aid in analyses of the previous, present, and future research directions of the NINCDS.

Epilepsy Advisory Committee. This chartered Committee provides advice to the Institute's Convulsive, Developmental, and Neuromuscular Disorders Program (CDNDP). It examines the changing state of science, reviews Program activities, and makes recommendations regarding future research requirements related to epilepsy. Recently the Committee has identified a need to improve the quality of epilepsy research and to increase the number of physician-scientists applying for NIH research funds as important objectives for the Institute. Ties between NINCDS and other organizations involved in epilepsy research and treatment (e.g., the Food and Drug Administration and the Veterans Administration) are considered to identify how the policies of one organization can bebetter coordinated with those of the others. The Committee also develops detailed recommendations for the types of future research that NINCDS should encourage. Both the Committee and the CDNDP keep careful track of the status of previous recommendations.

NEW PROJECTS PROPOSED

In addition to the many evaluation activities inherent in the conduct of the management of Institute research activities, the NINCDS will initiate in Fiscal Year 1986 a number of projects whose purpose is to evaluate and assess the Institute's scientific and programmatic efforts in a variety of key areas.

These new projects are described in a later section of this document.

National Institute of Neurological and Communicative Disorders and Stroke: Proposed Budget

			$ in Thousands		
			FY 85	FY 86	FY 87
NINCDS	82-302	Survey of Practice in the Management of Febrile Seizures	($10)	X	X
NINCDS	85-401	Assessment of New Directions in ALS Research 1/	(10)	X	X
NINCDS	85-402	Review of Research in Developmental Neurobiology (Two Projects)	(16)	X	X
NINCDS	85-403	Analysis of Research Re: the Prevalence of LAV Virus Antibodies in AIDS and pre-AIDS patients	--	X	X
NINCDS	85-404	International Review of Research in Auditory Biochemistry 2/	(14)	X	X
NINCDS	85-406	Head Injury Research Evaluation	(58)	X	X
NINCDS	85-407	Stroke Research Evaluation	(58)	X	X
NINCDS	85-409	Assessment of Need for Naturally-Occurring Animal Models of Human Neurological Disease 3/	(6)	X	X
NINCDS	85-410	Assessment of Neural Prostheses	(12)	(12)	(12)C
NINCDS	85-411	Assessment of Molecular Biology of Lysosomal Storage Disorders 4/	X	(10)	--
NINCDS	85-412	Assessment of Intensive Monitoring of Epileptic Seizures	X	(21)	--

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1/ Co-sponsored and funded with the Amyotrophic Lateral Sclerosis Society of America, the National Amyotrophic Lateral Sclerosis Foundation, and the Les Turner Foundation.

2/ Co-sponsored by the Association for Research in Otolaryngology.

3/ Co-sponsored with the assistance of the American College of Veterinary Pathologists.

4/ Co-sponsored and funded by the National Jewish Genetic Diseases Foundation.

				$ in Thousands	
			FY 85	FY 86	FY 87
NINCDS	85-413	Review and Analysis of Neuroimmunomodulation	(20)	X	X
NINCDS	85-414	Assessment of Research in Otolaryngology	(20)	--	X
NINCDS	85-415	Review of Impact of Neurobiology Research on Neurosurgery	(25)	--	--
NINCDS	86-401	Analysis of the Development of Social Cognition, Normal and Disordered, in Relation to the Diagnosis of Autistic Disorder	X	(10)	X
NINCDS	86-402	Evaluation of Protocol Design for Clinical Testing of Antiepileptic Drugs	X	(10)	X
NINCDS	86-403	Examination of Research on Chemical Reception and Chemical Irritants 5/	X	(20)	--
NINCDS	86-404	Review of Research on Presbycusis	X	C	X
NINCDS	86-405	Assessment of Studies Related to Development of Cochlear Implants	(8)	--	X
NINCDS	86-406	Assessment of Studies Related to Development of Communicative Devices for Non-Vocal Patients. 6/	X	C	X
NINCDS	86-407	Assessment of Communicative Prostheses for Pre-Lingual Deaf Children	(15)	--	X
NINCDS	86-408	Critical Review of Case-Control Studies of Risk Factors for Hearing and Tinnitus	X	(50)C	(50)C

5/ Co-sponsored and funded with the Association for Chemoreception Sciences.

6/ Co-sponsored and funded with the Deafness Research Foundation, the American Speech-Language-Hearing Association, et al.

			$ in Thousands		
			FY 85	FY 86	FY 87
NINCDS	86-409	Review of Studies on the Auditory Effects of Noise Publication	(15)	--	X
NINCDS	86-410	Assessment of Studies on Multiple Sclerosis 7/	(88)	--	X
NINCDS	86-411	International Review of the Use of Neural Prostheses for Motor Control 8/	(15)	--	X
NINCDS	86-412	Assessment of Brain Tumor Research and Therapy	X	(24)C	X
NINCDS	86-413	Review of Neurobehavioral Recovery from Head Injury	(26)	--	X
NINCDS	86-414	Review of Clinical Trials in MS	X	(4)	X
		Total FY 86 NINCDS Evaluation Fund Request		($161)	

NOTES:

( ) : Non-Set-Aside Funds
C : Conditionally Proposed
-- : Project Conducted but No Funds Needed From That Fiscal Year Budget
X : Project Not Conducted That Fiscal Year

7/ Co-sponsored by the National Multiple Sclerosis Society.

8/ Co-sponsored by: Paralyzed Veterans of America, American Paralysis Association, Engineering Foundation, Veterans Administration, National Institute of Handicapped Research, and the National Aeronautical and Space Administration.

New Projects Not Reviewed by NIH Technical Review Committee

NINCDS 86-401 - Analysis of the Development of Social Cognition, Normal and Disordered, in Relation to the Diagnosis of Autistic Disorder

This project is an effort to combine the expertise areas of the clinicians, the neurologists and the developmental psychologists in the evaluation and development of essential criteria for the diagnosis of Autistic Disorder. Currently, judgments of deviations from expected behavior are necessary for populations to be selected as "autistic," and the three professional disciplines are mutually unfamiliar with the knowledge available in each other's specialty areas. If progress is to be made in advancing knowledge of a disorder called "autism" in which developmentally impaired social relations are cardinal symptoms, then the separate spheres of knowledge of these three major disciplines must be brought to bear on the issue.

Estimated cost is approximately $10,000. Completion date is projected to be September 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-402 - Evaluation of Protocol Design for Clinical Testing of Antiepileptic Drugs

In the last several years there has been an increased interest in clinical trials of antiepileptic drugs, either for new drugs being developed, or uses of old drugs for new indications, e.g., post-traumatic epilepsy. Unfortunately serious problems in the design of trial protocols arise due to the nature of epilepsy and its current therapy. For example, most of the patients enrolled in clinical trials are those who have proven refractory to all previous medications, although the seizure frequency in these intractable cases varies widely among patients. Furthermore, most patients remain on at least one and sometimes two antiepileptic drugs during the clinical trial, so that the trial drug is never tested alone, and the patient is never drug free during the "placebo period." There is no unanimity of clinical or basic science opinion at the present time concerning the importance of the variables of seizure frequency or polytherapy in affecting the results of the trial, or how to design a protocol to minimize their influence, although many feel that current protocol design biases the trial against detecting efficacy. The proposed project would involve epileptologists, biostatisticians, the FDA, and representatives of pharmaceutical houses in an attempt to study the designs of a definitive clinical trial using state-of-the-art statistical and drug monitoring techniques. Once investigators have agreed upon the elements of a common protocol, not only would the quality of research applications and contract proposals be improved, but the adherence to protocols would probably be greater.

Estimated cost is approximately $10,000. Completion date is projected to be September 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-403 - Examination of Research on Chemical Reception and Chemical Irritants

A project is being planned with the Association for Chemoreception Sciences (AChems) to examine and evaluate research concerning common chemical reception and chemical irritants. The purpose of the project is to determine the possible need for greater stimulation of research in this area.

Estimated cost is approximately $20,000. Completion date is projected to be September 1987.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-404 - Review of Research on Presbycusis

This evaluative review is being planned for FY 1986 to focus on research in presbycusis, and specifically the use of non-human primate studies in this area. It will also focus on research areas concerning this disorder which need greater attention.

Estimated cost has not yet been determined. Completion date is projected to be September 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-405 - Assessment of Studies Related to Development of Cochlear Implants

FDA approval of a single-channel cochlear implant has renewed the urgency of a NINCDS-sponsored project to assess and establish the direction of program involvement in such studies as comparisons of different electrode arrays, pre-processors for speech stimuli and in studies related to the use of cochlear implants in children.

Estimated cost is approximately $7,500. Completion date is projected to be September 1987.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-406 - Assessment of Studies Related to Development of Communicative Devices for Non-Vocal Patients. A project co-sponsored with the Deafness Research Foundation, the American Speech-Language-Hearing Association,
et al.

A project is proposed to be co-sponsored by professional societies and voluntary associations to study the potential of research in the development of communicative devices for non-speaking patients.

Many different communicative devices have become available in recent years for augmenting or providing speech for patients either unable to speak or with unintelligible speech associated with a neurological disorder. Clinicians are in need of an evaluative system which would be useful for assessing patients' needs and capabilities and for interfacing these findings with the various device characteristics and use requirements.

Estimated cost for the project has not yet been determined. Completion date is projected to be September, 1987.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-407 - Assessment of Communicative Prostheses for Pre-Lingual Deaf Children

This project will provide an evaluation of research on the use of cochlear implants and other communicative prostheses for pre-lingual deaf children, and determine the possible need for greater stimulation of research.

Estimated cost is approximately $15,000. Completion date is projected to be December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-408 - Critical Review of Case-Control Studies of Risk Factors for Hearing and Tinnitus

This proposed project will be a critical review of available data on risk factors for hearing loss, to obtain an evaluation of all relevant national and international case-control studies that have explored the totality of the backgrounds of affected and unaffected persons. The results of each study will be evaluated to determine if the findings reflect the true situation with respect to the presence or absence of association between hearing impairment or tinnitus and the study factor(s) and if an association is observed, whether or not it is a causal one. In addition, a report of research needs on the epidemiology of hearing loss and tinnitus will be produced to be used as a guide for further program development in these areas. The long-term value of this work will be knowledge of the true size of the problem in order to determine funding requirements for clinical diagnosis and treatment as well as basic research efforts.

Estimated FY 1986 cost is approximately $50,000. Completion date is projected to be June 1988.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-409 - Review of Studies on the Auditory Effects of Noise Publication

This proposed project is designed to review and assess studies on the auditory effects of noise to determine validity and reliability of the studies and the procedures used. It will also attempt to determine the possible need for greater stimulation of research in this area.

Estimated cost is approximately $15,000. Completion date is projected to be October 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-410 - Assessment of Studies on Multiple Sclerosis

Co-sponsored and funded with the National Multiple Sclerosis Society, this project will review and assess research studies in the area of genetic, molecular and cellular aspects of demyelinative processes in multiple sclerosis.

Estimated cost is approximately $88,000. Completion date is projected to be December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-411 - International Review of Neural Prostheses Use for Motor Control

Co-sponsored and funded by numerous voluntary and professional organizations and other Federal agencies, this project will focus on a review and assessment of efforts concerning physical problems impeding development of devices to restore upper and lower extremity function to paralyzed patients, to assist respiration, and to correct scoliosis. Its goals are to uncover, discuss, and propose solutions to these problems, and secondly, to stimulate continuing review.

Estimated cost is approximately $15,000. Completion date is projected to be December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-412 - Assessment of Brain Tumor Research and Therapy

The purpose of this project is to review and evaluate information and existing knowledge in basic and clinical research on central nervous system neoplasms, emphasizing areas in which imminent progress is anticipated, such as: clinical and experimental therapy, tumor biology (including oncogenes and growth factors), CNS carcinogenesis, quantitative NS tumor imaging, and immunobiology of primary CNS tumors.

Estimated FY 1986 cost is approximately $24,000. Completion date is projected to be December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-413 - Review of Neurobehavioral Recovery from Head Injury

The aims of this project include a review of methodological problems and ambiguities in terminology which have complicated progress in the investigation of the neurobehavioral outcome of head injury. Recent publications concerning recovery from head injury and ongoing projects involving the collaboration of neuropsychologists and neurosurgeons have emphasized the difficulties in study designs and the application of neuropsychological tests. Limitations of global measures of outcome, the need for suitable measures of psychological functioning after head injury and appropriate tests to assess the effects of traumatic brain injury in children are among the unresolved methodological problems.

This project proposes to provide a critical appraisal of current progress and recommendations to clarify terminology and refine procedures in studying recovery from head injury. The long-term objective is to provide neurologists, neurosurgeons, psychiatrists and psychologists with a scientific foundation for the investigation of neurobehavioral recovery from head injury.

Estimated cost is approximately $26,000. Completion date is projected to be December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 86-414 - Review of Clinical Trials in Multiple Sclerosis (MS)

The purpose of this project is to review and assess the data and other information produced by clinical trials in multiple sclerosis as published in the past eight-year period with respect to statistical aspects of clinical experimentation considered important to valid treatment comparisons. It will also attempt to determine whether or not a redirection of emphasis is needed in future studies, either because past important findings have been left unexploited, or because current procedures have been shown to be unproductive. The number of drug trials in MS has increased over the last ten years, but it appears that many of these trials have statistical inadequacies, (e.g., small sample size, non-randomized, etc.) that may invalidate or at a minimum give ambiguous conclusions. The aim of this project is to examine a large number of MS clinical trials and describe, tabulate and evaluate their statistical properties.

Estimated cost is approximately $4,000. Completion date is projected to be December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

Status of Projects Proposed in Fiscal Year 1985 Evaluation Plan Not Reviewed by NIH Technical Review Committee

NINCDS 85-401 - Assessment of New Directions in ALS Research

Status: Completed, March, 1985

Co-sponsored and funded by three voluntary organizations (the Amyotrophic Lateral Sclerosis Society of America, the National Amyotrophic Lateral Sclerosis Foundation, and the Les Turner Foundation), the NINCDS conducted an evaluation of current research and research needs of system disorders such as motor neuron disease and various forms of ataxia, with a goal of generating new investigative approaches. This project produced models for the stimulation of new research areas which are currently neglected.

Estimated cost was approximately $10,000.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-402 - Review of Research in Developmental Neurobiology

Status: Project was Initiated; Will Continue in FY 1986

This included two projects, beginning in June 1984 and June 1985, which involve health voluntary organizations in reviewing and evaluating the clinical involvement and utilization of research results in developmental neurobiology.

Costs for the two projects are expected to total approximately $16,000.

It is expected that information resulting from these projects will be available by October 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-403 - Analysis of Research Re: the Prevalence of LAV Virus Antibodies in AIDS and Pre-AIDS Patients

Status: Completed, Fiscal Year 1985

This evaluative study was conducted by the Intramural Research Program to determine the efficiency and effectiveness of measures utilized in defining clinical neurological complications suffered by AIDS and pre-AIDS patients, with the aim of developing an effective methodology for defining the types of viral encephalopathy to which these patients may be subject.

Costs associated with this project were not separably identifiable within the Intramural Research Program. The project began in Fiscal Year 1984.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-404 - International Review of Research in Auditory Biochemistry

Status: Project was Completed in FY 1985

This project, which was co-sponsored by the Association for Research in Otolaryngology, was a two-year study of the research advances taking place in inner ear and central auditory system molecular biology to determine the applicability of recent research findings to treatment methods.

The estimated total cost for this two-year review was $35,000. Beginning in Fiscal Year 1984, and continuing into 1985, information from this project should be available by December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-405 - Review of Gene Localization Research in Selected Neurological Diseases

Status: Project was Cancelled

NINCDS 85-406 - Head Injury Research Evaluation

Status: Project was Completed in FY 1985

In Fiscal Year 1985 the NINCDS Stroke and Trauma Program awarded a grant for the development of a state-of-the-art paper on head injury research. This paper reviewed and evaluated progress, problems, and opportunities in this scientific area. Specific emphasis was be placed upon reviewing NINCDS programmatic activities and making recommendations for the future.

Costs for production of this paper were $58,000. The paper and further analysis of the issues presented should be available by December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-407 - Stroke Research Evaluation

Status: Project was Completed in FY 1985

The NINCDS Stroke and Trauma Program authorized and supported by grant in Fiscal Year 1985 the production of a state-of-the-art study paper on stroke research. This study reviewed and evaluated progress, problems, and opportunities in this scientific area. Specific emphasis was placed upon reviewing NINCDS programmatic activities and making recommendations for the future.

The cost for this project was $58,000. Analysis of the information contained in the paper should be available by December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-408 - Assessment of Terminology Utilization Relating to Cerebral Palsy

Status: Project was Cancelled

NINCDS 85-409 - Assessment of Need for Naturally-Occurring Animal Models of Human Neurological Disease

Status: Project was Completed in FY 1985

This project was co-sponsored with the assistance of the American College of Veterinary Pathologists to evaluate methodologies utilized to identify and develop animal models of human neurological disorders and/or to analyze and compare existing models for their relevance to the study of human disease. Clinical neuroscience would benefit from greater availability of animal models.

Costs for the study are estimated at $6,000. Information resulting from the project should be available by the end of 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-410 - Assessment of Neural Prostheses

Status: Project was Initiated in FY 1985; Will Continue in FY 1986

This project is sponsored by the Fundamental Neurosciences Program to ascertain the potential for the development of neural prostheses which would provide stimulation of sensory centers in the central nervous system, based on current technology and practices.

FY 1985 funding for this study was $12,000. Resulting information should be available by December 1985.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-411 - Assessment of Molecular Biology of Lysosomal Storage Disorders

Status: Project was Postponed; Will Begin in FY 1986

This project is co-sponsored and funded by the National Jewish Genetic Diseases Foundation. The object of the study is to examine and evaluate for efficacy the mechanisms and techniques utilized in gene cloning and investigations of the lysosomal enzyme process.

The level of support by NINCDS is projected to be $10,000. The study results will be published and should be available by July 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-412 - Assessment of Intensive Monitoring of Epileptic Seizures

Status: Project was Postponed; Will Begin in FY 1986

This study, which will be conducted via grant, will review and evaluate the present status of, and future opportunities for, research in the mechanisms of epilepsy.

Estimated costs for the study are projected to be $21,000. Information resulting from the study should be available by March 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-413 - Review and Analysis of Neuroimmunomodulation

Status: Project was Completed in FY 1985

This project analyzed and evaluated the methodologies and techniques utilized in neuroimmunomodulation research to determine reliability and efficacy. The study determined those approaches and techniques which are most reliable and effective in this area of research.

Costs of this study were $20,000.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-414 - Assessment of Research in Otolaryngology

Status: Project Will Be Conducted in FY 1986

The Communicative Disorders Program plans to conduct a review and evaluation of research goals and methods in otolaryngology, with an objective of determining those research areas which need greater clinician involvement in order to facilitate the transfer of research findings into the clinical realm.

It is estimated that the costs of this project will be approximately $20,000. Information resulting from this assessment should be available by March 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

NINCDS 85-415 - Review of Impact of Neurobiology Research on Neurosurgery

Status: Project was Initiated in FY 1985; Will Continue in FY 1986

The Fundamental Neurosciences Program plans a review and assessment of the impact of research in neurobiology on the clinical practices of neurosurgery. Results of this review will assist in determining which areas of neurobiology research need greater clinical involvement to promote knowledge transference to clinical practice.

This multi-year initiative is projected to cost approximately $25,000 in Fiscal Year 1985 funds. Information resulting from this study should be available by December 1986.

No data collection subject to the Paperwork Reduction Act of 1980.

Project No.: NINCDS 82-302

1. **EDC ID No.:** 2144
2. **Entry Dates:**
3. **Status:** Completed
4. **Project Title:** Survey of Practice in the Management of Febrile Seizures
5. **Report Title:** Survey on the Management of Febrile Seizures
6. **Agency Sponsor:** PHS-NIH-NINCDS
7. **Start/End Dates:** 82-06; 85-05
8. **Performer:** Office of Biometry and Field Studies, National Institute of Neurological and Communicative Disorders and Stroke
   7550 Wisconsin Avenue, Bethesda, MD 20205
9. **Agency Contact:** Young Jack Lee, Ph.D.; Federal Building, Room 7C108
   301-496-4795
10. **Cost:** FY 82: $4 FY 83: $24 FY 84: $15 FY85: ($10)
11. **Fund Source:** Evaluation
12. **Mechanism:** In-house
13. **Project No.** NINCDS 82-302
14. **Contract No.:** Z01 NS 02412-03
15. **NTIS No.:** N/A
16. **ERIC No.:** N/A
17. **Program(s) Evaluated:** PHS-NIH Biomedical Research-Institute Specific-Neurological, Communicative Disorders and Stroke
18. **Evaluation Type:** Assessment of national (research) programs
19. **Descriptors:** Neurological disorders, febrile seizures, infants and young children, prophylaxis, sequelae, prognosis, risk factors, side effects, anticonvulsants, current practice
20. **Abstract:** Major advancements in understanding the natural history of febrile seizures have been made in the last decade. This survey identified current practices in the management of febrile seizures.

    The survey assessed the frequency with which each physician cares for febrile seizure children, how often they prescribe anticonvulsant medication, and how often they seek consultation. It also determined physicians' rationales for deciding how to treat children who have had febrile seizure(s) and the goals of any treatment. The most preferred medications and contingencies for treatment of side effects were determined. Questions on current practice in monitoring blood drug levels and hospitalizing the febrile seizure child were included in the survey.

Ten thousand physicians in general/family practice, neurology and pediatrics were sent an anonymous questionnaire without any hidden identifiers. Data analysis, report writing, and all mailings are completed, and data has been processed. The return rate was approximately 70 percent.

Statistical analyses of the resulting data include cross-classification and tabulations. Recommendations resulting from the study will be made on future directions and priorities for febrile seizure research.

Project No.: NINCDS 83-301

1. **EDC ID No.:** 2133
2. **Entry Dates:**
3. **Status:** Completed
4. **Project Title:** Survey of Antiepileptic Drug Use
5. **Report Title:** Study of Antiepileptic Drug Usage
6. **Agency Sponsor:** PHS-NIH-NINCDS
7. **Start/End Dates:** 83-09; 84-08
8. **Performer:** MANDEX, Inc.
9. **Agency Contact:** Frank J. Nice, Federal Building, Room 114, 301-496-6691
10. **Cost:** FY 83: $114
11. **Fund Source:** Evaluation
12. **Mechanism:** Contract
13. **Project No.** NINCDS 83-301
14. **Contract No.:** N01-NS-3-2354
15. **NTIS No.:** X-NYD
16. **ERIC No.:** N/A
17. **Program(s) Evaluated:** PHS-NIH Biomedical Research-Extramural Research-NINCDS-Antiepileptic Drug Development Program (ADDP)
18. **Evaluation Type:** Program Impact
19. **Descriptors:** Drug Therapeutics and Devices
20. **Abstract:** The prescribing and dispensing of specific antiepileptic drugs were estimated nationally. The types and frequencies of seizures for which the drugs are prescribed were estimated. These data will provide the ADDP and the NINCDS with information about areas in which new drugs are needed as well as the impact of drugs recently introduced. The results will also provide a baseline reference value against which to measure changes in availability and use of particular antiepileptic drugs in three to five years. Two distinct data collection techniques were utilized. First, a survey of organizations in which drugs are dispensed and prescribed was performed. Organizations included were drug wholesalers, hospitals, and pharmacies. Secondly, physicians who treat patients with seizures were also surveyed. Data derived by each technique were linked to provide information on amounts of antiepileptic drugs being used and the number of patients with refractory seizures which persist in spite of available drugs. Study results were disseminated by means of a final contract report. The RFP was issued in April 1983 with proposals due June 15, 1983. The Technical Merit Review was July 22, 1983, and the Contract Review Board was held on August 15, 1983. The contract was awarded September 1983 and completed with the submission of the final report on July 25, 1984.

15

NATIONAL LIBRARY OF MEDICINE

Dr. Donald A. B. Lindberg, Director

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National Library of Medicine: Proposed Budget

	$ in Thousands		
	FY 85	FY 86	FY 87
NLM 80-401 Evaluation of Medical Library Resource Project Grant Program	--	--	--
NLM-80-402 Consultant Review of Lister Hill Center Programs	(10)	(10)	(10)
NLM 80-404 Medical Library Assistance Act Program Performance Evaluation	--	(8)	--
NLM 83-401 Assessment of CHEMLINE	--	--	--
NLM 84-402 Analysis of Interlibrary Loan - Requests for Serial Services	(5)	--	--
NLM 86-401 Field Test and Evaluation of the MEDLINE Optical Disk (MOD) System	--	(75)	--
Total FY86 NLM Evaluation Fund Request		(93)	

Reviewed and approved by
NIH Technical Review Committee

1. NIH Evaluation Project Identifier: NLM-86-401

2. Project Title and Capsule Description:

   a. Title: Field Test and Evaluation of the MEDLINE Optical Disk (MOD) System.

   b. Capsule Description: Contemporary computer technology and mass storage devices make it physically and economically feasible to store and retrieve large quantities of information in forms and formats directly accessible by health professional end-users and intermediary searchers. The National Library of Medicine (NLM) is undertaking an experiment in which the NLM's MEDLINE bibliographic database will be made available in a local processing mode, using a state-of-the-art microcomputer driven optical disk system developed by an external vendor. The proposed project will field test and evaluate the technical performance, user acceptance, and cost effectiveness of the MOD System (MEDLINE on Optical Disk) alone and in comparison with the standard MEDLINE system which operates on an NLM host computer accessible via telecommunications networks.

3. Cost and Funding Source:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
1986	($75)	--	($75)

The budgeted amount is intended to cover expenses associated with data collection at 3-5 test sites; including the part-time services of staff assisting in the project at their institutions.

4. Project Monitor/Contact: Elliot R. Siegel, Ph.D., Special Assistant for Operations Research, Office of Planning and Evaluation, NLM, Building 38, Room 2S-18, (301) 496-8834.

5. Coordination: This project has been reviewed by NLM's Director, Deputy Director for Research and Education, Associate Director for Planning and Evaluation, and Associate Director for Library Operations.

6. Program Evaluated: PHS-NIH-Biomedical Research-Library of Medicine.

7. Intended User: Intended users of the information are the senior staff of the National Library of Medicine (NLM).

8. Information to be Generated: The proposed project will evaluate the technical performance, user acceptance, and cost effectiveness of a state-of-the-art microcomputer driven optical disk system designed to provide users of computerized bibliographic databases with a stand alone search and retrieval capability. Such systems hold the promise of significantly enhancing access to the latest biomedical information by enabling health professional end-users,

as well as intermediary searchers, to perform retrievals on large computerized bibliographic databases using relatively inexpensive, locally maintained and operated hardware and software.

The evaluation will generate information on the MOD System alone, and in comparison with the standard MEDLINE bibliographic retrieval system now used to conduct some 2 1/2 million searches annually. Variables to be studied may be grouped into 3 areas and include the following:

a. Technical Performance--Versatility/power of retrieval system; reliability of system; response time; display characteristics; and design features of the user-system interface.

b. User Acceptance--Perceived ease of system use; user satisfaction with display alternatives; user satisfaction with online instructions, prompts, help messages; user satisfaction with training; observable changes in searching behavior and/or search strategies as a function of user experience.

c. Cost Effectiveness--Costs in terms of dollars, time, and effort of performing searches of varying types as a function of perceived effectiveness of search outcome. Cost benefits of health professionals performing their own searches without the aid of a search intermediary is an especially important issue that will be addressed.

Results of this study will also be used to determine NLM licensing and pricing arrangements with organizations desiring to vend MEDLINE services utilizing this new technological medium.

9. Approach: The proposed field test and evaluation will be carried out at 3-5 institutions, including the NLM's own reading room, that are representative of hospital and medical library users of MEDLINE. The MOD System, consisting of a monthly-updated optical disk containing the MEDLINE database, a disk player, microcomputer and search system software, will be installed at each test institution for a period of 6 months. On-site staff will be trained in its operation and maintenance. Protocols will be established for carrying out controlled field experiments that take into account each institution's organizational structure and customary mode of providing MEDLINE searches to patrons and staff. Methodology will be based upon procedures, survey instruments and structured interview forms previously developed by NLM in conjunction with an in-house comparative evaluation of two online catalog systems (Siegel et. al., 1984); and which are currently in use by other investigators in a nation-wide study of computerized library catalogs (Markey, 1984). They include verification and limits testing which will determine and document the extent to which the MOD System meets the technical performance requirements as specified. User acceptance will be addressed by three complementary data collection strategies: a Sample Search Experiment designed to provide control over potentially confounding variables, a Comparison Search Experiment intended to maximize the authenticity of study

conditions, and a User Survey characterizing system users' information needs and searching behavior.

10. Information Clearance/Collection: Yes.

11. Prerulemaking Activity: None

12. References:

Markey, K.: The Dewey Decimal Classification as a library user's tool in an online catalog. Proceedings of the 47th Annual Meeting of the American Society for Information Science, October 1984, Philadelphia, PA., White Plains, N.Y.: Knowledge Industry Publications.

Siegel, E.R., Kameen, K., Sinn, S.K., and Weise, F.O.: A comparative evaluation of the technical performance and user acceptance of two prototype online catalog systems. Information Technology and Libraries, March 1984, 3(1), 35-46.

Project No. NLM-80-401

1. EDC ID No.: 1792

2. Entry Dates:

3. Status: In Process

4. Project Title: Evaluation of Medical Library Resource Project Grant Program

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NLM

7. Start/End Dates: 79-11, NYD

8. Performer: NLM-Extramural Programs, 8600 Rockville Pike, Bethesda, MD 20209

9. Agency Contact: Richard T. West, Building 38A, Room 5S-504, 496-3113

10. Cost: FY 1981-($8), FY 82-($8), FY 83-($8), FY 84-(0), FY 85-(0), FY 86-(0)

11. Fund Source: Institute

12. Mechanism: In-house

13. Project No.: NLM-80-401

14. Contract No.: NA

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Library of Medicine

18. Evaluation Type: Program Impact

19. Descriptors: Library Services, Information Systems

20. Abstract: Evaluation of the Medical Library Resource Project Grant Program, one of the NLM Extramural Programs authorized by the Medical Library Assistance Act. From 1971 to 1980 approximately $16.5 million dollars has been expended in almost 950 awards to health science libraries for the purpose of improving information service activities. The evaluation will determine program impact, identify areas of program modification, if any, and recommend future program activity. Results will assure continued development of needed health information services and systems in the Nation's health science libraries.

A similar evaluation was completed in 1975 for the Medical Library Resource Improvment Grant program, companion program to the Library Project Grant under MLAA authority. Results were reported and the program modified to be more responsive to current needs.

Project No.: NLM 80-402

1. EDC ID No.: 1793
2. Entry Dates:
3. Status: In Process
4. Project Title: Consultant Review of Lister Hill Center Program
5. Report Title: X-NYD
6. Agency Sponsor: PHS-NIH-NLM
7. Start/End Dates: 79-10, NYD
8. Performer: National Library of Medicine, Lister Hill National Center for Biomedical Communications, 8600 Rockville Pike, Bethesda, MD 20209
9. Agency Contact: Earl Henderson, Bldg. 38A, Rm 7N711, 496-4441
10. Cost: FY 1984 (10), FY 1985 (10), FY 1986 (10), FY 1987 (10)
11. Fund Source: Institute
12. Mechanism: In house P.O.
13. Project No.: NLM 80-402
14. Contract No.: NA
15. NTIS No.: NA
16. ERIC No.: NA
17. Program(s) Evaluated: PHS-NIH-Biomedical Research Library of Medicine
18. Evaluation Type: Program Strategy
19. Descriptors: Library Services, Information Systems
20. Abstract: The Board of Scientific Counselors of the NLM was established in 1981 to review the research and development programs of the Library primarily those of the Lister Hill National Center for Biomedical Communications. Initial reviews at the broad research program level identified the programs as basically sound. Recent meetings have included review of additional programs and in depth review of proposed new project research. The reviews are conducted with the participation of the Board of Regents, and other consultants when they are required. Advice is presented to NLM management and staff during the regular meetings and as reports included with the minutes of the Board.

Project No. NLM-80-404

1. EDC ID No.: 1795

2. Entry Dates:

3. Status: In Process

4. Project Title: Medical Library Assistance Act Program Performance Evaluations

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NLM

7. Start/End Dates: 76-10, NYD

8. Performer: NLM Extramural Programs, 8600 Rockville Pike, Bethesda, MD 20209

9. Agency Contact: Richard West, Building 38A, Room 5S-504, 496-3113

10. Cost: FY 77-($16), FY 81-($8), FY 82-($16), FY 83-($8), FY 84-($8) FY 86-($8)

11. Fund Source: NLM Account

12. Mechanism: In-house

13. Project No.: NLM-80-404

14. Contract No.: NA

15. NTIS No.: X-NYD

16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Library of Medicine

18. Evaluation Type: Program Impact

19. Descriptors: Library Services, Information Systems

20. Abstract: NLM has six grant programs authorized by the Medical Library Assistance Act (MLAA) of 1965, as amended. They are:

- Research Grants
- Training Grants
- Publication Grants
- Special Scientific Project Grants
- Resource Project Grants
- Resource Improvement Grants

Program performance evaluations have been conducted, are underway, or are planned for each of these grant programs.

The general approach for these studies has been to use in-house staff supplemented by consultants as appropriate. More detailed information will be contained in program performance summaries to be prepared for each grant program.

1. EDC ID No.: 2097 Project No.: NLM 82-303

2. Entry Dates: 3. Status: Completed

4. Project Title: Study of Audiovisual Selection-Acquisition Process

5. Report Title: A Study of the Audiovisual Selection and Acquisition Process in Health Professions Education.

6. Agency Sponsor: PHS-NIH-NLM 7. Start/End Dates: 82-07, 85-5

8. Performer: U. of Iowa, Office of the Vice. Pres. for Educational Devel. & Research, Div. of Sponsored Programs, 100 Gilmore Hall, Iowa City, Iowa 52242

9. Agency Contact: Warren F. Seibert, Ph.D., Bldg. 38A, Rm 9N905, 496-9300

10. Cost: FY82-109; FY 84-32

11. Fund Source: Evaluation 12. Mechanism: Contract

13. Project No.: NLM 82-303 14. Contract No.: N01-LM-2-3511

15. NTIS No.: PB86-108131/GBB 16. ERIC No.: NA

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Library of Medicine

18. Evaluation Type: Program Strategy

19. Descriptors: Educational technology, survey or questionnaire feature, statistical analysis methods feature, health manpower training, education manpower, education techniques.

20. Abstract: This study investigated the information and processes that health professions educators use in identifying and selecting AV instructional materials. It was designed to identify the information sources that educators and resource consultants use; to study the role of information sources, including NLM's AVLINE, in the materials selection process; and to compare these findings with two related sets of findings gleaned from the professional literature, i.e., the processes used by health professions educators in identifying and selecting printed instructional materials, and the processes used by educators outside the health professions in identifying and selecting AV instructional materials. The project's literature review was completed in September, 1983, OMB approval for the field survey was received in February, 1984, and the survey was conducted in the fall of that year. The survey data were analyzed during the early months of CY 1985 and the project's draft final report was completed and submitted in May, 1985. This report provides extensive data describing audiovisual materials selection and utilization practices in health professions education, and NLM's role in this process.

Project No. NLM-83-401

1. EDC ID No.: 2380

2. Entry Dates:

3. Status: In Process

4. Project Title: Assessment of Chemline

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NLM

7. Start/End Dates: 84-06/85-12

8. Performer: NLM, 8600 Rockville Pike, Bethesda, MD 20209

9. Agency Contact: Dr. Melvin Spann, SIS/NLM, Bldg. 38A, Rm. 3S319
Dr. Elliot Siegel, OD/NLM, Bldg. 38, Rm. 2S18

10. Cost: FY 1985 - ($15) FY 1986 ($0)

11. Fund Source: Institute

12. Mechanism: In-house & P.O.

13. Project No.: NLM-83-401

14. Contract No.: N.A.

15. NTIS NO.: X-NYD

16. ERIC No.: NL

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Library of Medicine

18. Evaluation Type: Program Impact

19. Descriptors: Library Services, Information Systems, Information Dissemination; Chemical Information

20. Abstract: CHEMLINE (CHEMical Dictionary onLINE) is the interactive dictionary maintained by the Specialized Information Services Division of the National Library of Medicine (NLM). It provides a mechanism for searching over 600,000 chemical substances online and retrieving CAS Registry Numbers, molecular formulae, Chemical Abstracts index nomenclature, and generic names and synonyms. CHEMLINE provides a locator designation that points to other files in the NLM's MEDLARS (MEDical Literature Analysis and Retrieval System) system that contain information on a particular chemical substance.

The purpose of this evaluation of CHEMLINE is to provide data that will assist the NLM in making decisions concerning future developments of CHEMLINE. The study will address CHEMLINE's ability to fulfill current user needs and its potential for responding to future user requirements.

Project No. NLM-84-401

1. EDC ID No.:

2. Entry Dates: 3. Status: Complete

4. Project Title: Evaluation of HISTLINE Database

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NLM 7. Start/End Dates: 84-01, 85-04

8. Performer: History of Medicine Division

9. Agency Contact: John Parascandola, History of Medicine Division, Library Operations, NLM

10. Cost: FY 1984-($5); FY 1985-($5)

11. Fund Source: Institute 12. Mechanism: In-house

13. Project No.: NLM-84-401 14. Contract No.: N/A

15. NTIS No.: X-NYD 16. ERIC No.: N/A

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Library of Medicine-Library Operations-History of Medicine Division-HISTLINE Database

18. Evaluation Type: Program Impact

19. Descriptors: Library Services, History of Medicine, Online retrieval systems

20. Abstract: This project is an analysis of the content of the HISTLINE database, which addresses type of citation (e.g., journal article, monograph, thesis), source of citation, and subject, language, and geographic characteristics of the citation. Results of the analysis were reported in a paper by James Kopp entitled "Research and Writing in the History of the Health Sciences, 1970-1982: A Quantitative Analysis of NLM's HISTLINE Database" given at meetings of the Washington Society of the History of Medicine and the Medical Library Association and recently published in the Bulletin of the Medical Library Association.

A planned analysis of the usage of the database has been deferred indefinitely.

Project No. NLM-84-402

1. EDC ID NO.: 2394

2. Entry Dates: 3. Status: In Process

4. Project Title: Analysis of Interlibrary Loan Requests for Serial Services

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-NLM 7. Start/End Dates: 84-01, 85-09

8. Performer: Circulation and Control Section, Reference Services Division, Library Operations, NLM

9. Agency Contact: Jacque-Lynne Schulman, Building 38, Room B1E-23B, 496-5511

10. Cost: FY 1984-($5); FY 1985-($5)

11. Fund Source: Institute 12. Mechanism: In-house

13. Project No.: NLM-84-402 14. Contract No.: N/A

15. NTIS No.: X-NYD 16. ERIC No.: N/A

17. Program(s) Evaluated: PHS-NIH-Biomedical Research-Library of Medicine-Library Operations-Reference Services Division-Interlibrary Loan

18. Evaluation Type: Program Impact

19. Descriptors: Library Services, Interlibrary Loan

20. Abstract: This project is an examination of the origin, magnitude and characteristics of interlibrary loan demand for serials and NLM's current response to the network needs which they reflect. Findings will provide data to improve program management and efficiency through a description and analysis of requesting institution characteristics and needs, correlated with NLM's ability to respond in ways to satisfy those needs. Indepth analysis will be made of interlibrary loan requests for serials received at NLM in its role as backstop to the Regional Medical Library Network. Data collection is a byproduct of ongoing automated production. Approximately 100,000 serial requests representing 100% of those received for a six-month period constitute the data for analysis. The primary target group is the NLM Library Operations management staff and the method of study dissemination will be a written report. A preliminary report has been produced and reviewed and is now being expanded to provide data comparable to an earlier comprehensive study of serial interlibrary loan requests received by NLM in 1959.

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DIVISION OF RESEARCH RESOURCES

Dr. Betty H. Pickett, Director

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List of Projects and Proposed Budget 16.3

Evaluation Documentation Center Forms for Continuing and Recently Completed Projects 16.5

Division of Research Resources: Proposed Budget

		$ in Thousands FY 85	 FY 86	 FY 87
DRR 80-401	Major Clinical Applications of Research Findings Accomplished at General Clinical Research Centers (GCRCs)	--	--	--
DRR 85-403	Outcome Study of the Clinical Associate Physician (CAP) Program	--	--	--
	Total FY 86 DRR Evaluation Fund Request		$0	

Project No.: DRR 80-401

1. EDC ID No.:

2. Entry Dates:

3. Status: In Process

4. Project Title: Major Clinical Applications of Research Findings Accomplished at General Clinical Research Centers (GCRCs)

5. Report Title: Advances in Diabetes, December 1982
Advances in Neuroendocrine Sciences, March 1983
Advances in Perinatology, March 1983
Advances in Hypertension, May 1983

6. Agency Sponsor: PHS-NIH-DRR

7. Start/End Dates: 79-11, NYD

8. Performer: In-House Project

9. Agency Contact: Eric C. Elliot, M.D., Ph.D.
Building 31, Room 5847
(301) 496-6595

10. Cost: NA

11. Fund Source: Research

12. Mechanism: Internal

13. Project No.: DRR 80-401

14. Contract No.: NA

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Research Resources

18. Evaluation Type: Research and Data Development

19. Descriptors: Ambulatory and Outpatient Health Care, Bibliography Feature, Biomedical Research, Chronic Disease, Communicable Disease, Diabetes, Digestive and Metabolic Disease, Drugs Therapeutic and Devices, Food and Nutrition, Health Care Techniques, Heart Disease, Infants, Literature Review Feature, Neurology, Technology Assessment or Transfer

20. Abstract: This project was undertaken in order to examine the contribution of the Division of Research Resources' GCRCs over the past 20 years to major clinical applications of research findings. The GCRC Program Advisory Committee identified areas of significant medical advances and a group of expert consultants then examined pertinent publications in the chosen areas which emanated from GCRCs. The expert consultants provided judgment on the most significant publications, and from their reports the four reports summarizing advances in the four areas were prepared, highlighting the GCRC contributions. A report on nutrition, the next selected topic, is due for completion late in 1985.

Project No.: DRR 84-401

1. EDC ID No.: 1526

2. Entry Dates:

3. Status: Complete

4. Project Title: Evaluation of the Activities of the Biomedical Research Technology Program in the Area of Mass Spectrometry

5. Report Title: Report of the Mass Spectrometry Task Force to the Biotechnology Resources Review Committee

6. Agency Sponsor: PHS-NIH-DRR

7. Start/End Dates: 84-03, 84-09

8. Performer: In-House Project

9. Agency Contact: Charles L. Coulter, Ph.D.
Building 31, Room 5B41
(301) 496-5411

10. Cost: NA

11. Fund Source: Research

12. Mechanism: Internal

13. Project No.: DRR 84-401

14. Contract No.: NA

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Research Resources

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research, Federal Role, Planning

20. Abstract: A panel of mass spectrometry experts, biochemists, and biologists was brought together to provide advice and information relevant to Program decisions regarding the commitment of limited funds in a manner most likely to contribute technological support to important biological and medical research problems. There have been many advances in high molecular weight mass spectrometry in recent years, and the panel explored ways to facilitate the expansion of the applicability of MS capabilities.

The Panel concluded that most biochemists were not aware of the new capabilities of mass spectrometry and that not enough high mass instruments are available. They recommended that time-of-flight based commercial systems be placed in biochemical laboratories to evaluate their usage; that more magnetic sector instruments be made available; and, that overall systems development be supported in time-of-flight and fourier transform mass spectrometry.

Project No.: DRR 85-401

1. EDC ID No.:

2. Entry Dates: 3. Status: Complete

4. Project Title: Evaluation of the Need for Supercomputer Access

5. Report Title: No report issued

6. Agency Sponsor: PHS-NIH-DRR 7. Start/End Dates: 84-03, 84-12

8. Performer: In-House Project

9. Agency Contact: Jack Hahn, Ph.D.
Building 31, Room 5B43
(301) 496-5411

10. Cost: NA

11. Fund Source: Research 12. Mechanism: Internal

13. Project No.: DRR 85-401 14. Contract No.: NA

15. NTIS No.: NA 16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Research Resources

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research, Federal Role, Information Processing, Planning

20. Abstract: A panel of 10 non-NIH scientists, at the invitation of the Biomedical Research Technology Program (BRTP), attended a three-day workshop on supercomputers sponsored by the National Science Foundation. At the conclusion of the workshop, the panel met with BRTP staff to address the use of supercomputers--present and proposed--in biology and medicine. The panel also made recommendations regarding the possible role of the BRTP in providing support to biomedical investigators for supercomputing access and training in the context of overall NIH involvement in this area, and considered the special problems of making supercomputers accessible to biological scientists including developing and adapting software and providing network accessibility.

The panel confirmed that biomedical research would benefit from access to supercomputers (e.g., image processing, large complex simulations, molecular dynamics), and that the BRTP has a role and responsibility in this area. They also stressed the need for support to assist biomedical scientists in developing and adapting software and making the other arrangements necessary to transfer their work to a supercomputer.

Project No.: DRR 85-402

1. EDC ID No.:

2. Entry Dates:

3. Status: Complete

4. Project Title: Evaluation of the Biomedical Research Technology Small Grant Program

5. Report Title: No Report Issued

6. Agency Sponsor: PHS-NIH-DRR

7. Start/End Dates: 84-04, 84-12

8. Performer: In-House Project

9. Agency Contact: Charles L. Coulter, Ph.D.
Building 31, Room 5B41
(301) 496-5411

10. Cost: NA

11. Fund Source: Research

12. Mechanism: Internal

13. Project No.: DRR 54-402

14. Contract No.: NA

15. NTIS No.: NA

16. ERIC No.: NA

17. Program Evaluated: PHS-NIH-Biomedical Research-Research Resources

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research, Federal Role, Planning

20. Abstract: The Biomedical Research Technology Program initiated a small grant award beginning with the February 1 application receipt date in 1983. This is a one-year, non-renewable award for pilot projects in high technology, engineering, instrumentation, physics, or computer science related to biomedical research. The projects involve feasibility studies of innovative and high-risk ideas and provide a basis for more extended research in the project's technology.

Using data gathered from grantees and non-NIH scientists who reviewed applications, DRR staff and advisors met to discuss the limited experience had with the Program so far in order to consider various options for change in its operations. The major recommendations were that the Program be continued, and that the maximum award be raised from $15,000 to $25,000 in direct costs.

Project No.: DRR 85-403

1. EDC ID No.:

2. Entry Dates:

3. Status: In Process

4. Project Title: Outcome Study of the Clinical Associate Physician (CAP) Program

5. Report Title: NYD

6. Agency Sponsor: PHS-NIH-DRR

7. Start/End Dates: 85-03, 86-NYD

8. Performer: In-House

9. Agency Contact: Eric C. Elliot, M.D., Ph.D.
Building 31, Room 5B47
(301) 496-6595

10. Cost: NA

11. Fund Source: Research

12. Mechanism: Internal

13. Project No.: DRR 85-403

14. Contract No.: NA

15. NTIS No.: NYD

16. ERIC No.: NA

17. Program Evaluated: PHS-Biomedical Research-Research Resources

18. Evaluation Type: Program Strategy

19. Descriptors: Biomedical Research, Federal Role, Planning, Scientific Manpower

20. Abstract: Since 1974, the CAP Program has been implemented at DRR's General Clinical Research Centers (GCRCs). A CAP award is funded as a competitive supplement to a GCRC grant on behalf of a young academic scholar, trained in patient care and research through the fellowship level or its equivalent, who is developing a career in clinical investigation by working on the GCRC. By supplementing professional-level patient care of Center patients, providing Core Laboratory direction and assistance, or performing supervisory and instructional duties, the CAP develops into an independent investigator under the supervision of the Program Director.

The primary purpose of the CAP Program is to produce independent clinical investigators by providing support early in their research careers. In fiscal year 1986, a report summarizing the history, operation, and present status of the CAP program will be produced--possibly as a journal article. Among the data to be examined for CAP Program participants will be their current occupations/activities; their success rate in obtaining independent NIH grant support; and their publication records.

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FOGARTY INTERNATIONAL CENTER

Craig K. Wallace, M.D., Director

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List of Projects and Proposed Budget 17.3

Evaluation Documentation Center Forms for Continuing Projects 17.5

Fogarty International Center: Proposed Budget

		$ in Thousands FY 85	 FY 86	 FY 87
FIC 82-301	Evaluation of FIC Senior International Fellowship Program	$ --	$ --	$ --
FIC 85-401	Assessment of Scientific and Professional Accomplishments of Former International Research Fellows	--	(150)	--
Total FY 86 FIC Evaluation Fund Request			(150)	

NOTE:

( ) non set-aside funds

Project No. FIC 82-301

1. EDC ID No.: 2148
2. Entry Dates:
3. Status: Ongoing
4. Project Title: Evaluation of Senior International Fellowship Program (SIFP)
5. Report Title: X-NYD
6. Agency Sponsor: PHS-NIH-FIC
7. Start/End Dates: 83-5, 85-12
8. Performer: Policy Analysis, Inc.
9. Agency Contact: Coralie Farlee, Ph.D.
Fogarty International Center
Building 38A, Room 605
301-496-1491
10. Cost: FY83 - $158
11. Fund Source: Evaluation
12. Mechanism: Contract
13. Project No.: FIC 82-301
14. Contract: N01-TW-3-2109
15. NTIS No.: X-NYD
16. ERIC No.: NA
17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Fogarty International Center-FIC International Research Fellowship Program
18. Evaluation Type: Program Impact Study
19. Descriptors: International issues, scientific manpower, health manpower training, educational administration
20. Abstract: This evaluation project is intended to assess the impact of six years of the Senior International Fellowship Program. The goals of the project are to determine:

    1. the impact of the fellow on the host laboratory;
    2. the impact of the experience in the foreign laboratory on the fellow (e.g., knowledge, research technology, concepts, continuing collaboration, etc.);
    3. the impact on the U.S. (home) institution (e.g., how the experience has affected the fellow's research, teaching, etc.)

Project No. FIC 85-401

1. EDC ID No.:

2. Entry Dates: 3. Status: Ongoing

4. Project Title: Assessment of Scientific and Professional Accomplishments of Former International Research Fellows

5. Report Title: X-NYD

6. Agency Sponsor: PHS-NIH-FIC 7. Start/End Dates: 85-12, 87-12

8. Performer: X-NYD

9. Agency Contact: Coralie Farlee, Ph.D.
Fogarty International Center
Building 38A, Room 605
301-496-1491

10. Cost: FY 86-($150)

11. Fund Source: FIC 12. Mechanism: Contract

13. Project No.: FIC 85-401 14. Contract: N01-TW-

15. NTIS No.: X-NYD 16. ERIC No.: NA

17. Programs(s) Evaluated: PHS-NIH-Biomedical Research-Fogarty International Center-FIC International Research Fellowship Program

18. Evaluation Type: Program Impact Study

19. Descriptors: International issues, scientific manpower, health manpower training, educational administration

20. Abstract: Scientific and professional accomplishments of former international research fellows will be assessed and documented. Approaches will be developed to (1) conduct literature searches and to (2) design the sampling plan. Information on professional status and scientific accomplishments will be collected. A system will be developed to maintain current follow up information on fellows in future years.

GUIDANCE FOR PREPARATION OF THE
FY 1986 NIH EVALUATION PLAN

Program Evaluation Branch
Office of the Director, NIH

March 1985

GUIDANCE FOR PREPARATION OF THE FY 1986 NIH EVALUATION PLAN

Introduction

The NIH Evaluation Plan for FY 1986 will be developed using basically the same procedures as last year. the only differences are:

1. Concept review by the NIH Evaluaton Oversight and Policy Committee usually will occur before technical review by the NIH Evaluation Technical Review Committee.
2. The Project Description and Justification form has been revised slightly.

The due date for NIH plan submissions to OASH is July 2. Therefore, it is important that each BID meet the OD/OPPE due dates listed below:

Institute	Set-aside PDJ Due	Initial Draft Due Date	Budget Tables, EDC Forms, and Revisions Due
NCI	May 1	May 16	June 17
NEI	May 1	May 9	June 17
NHLBI	May 1	May 16	June 17
NIA	May 1	May 9	June 17
NIADDK	May 1	May 9	June 17
NIAID	May 1	May 16	June 17
NICHD	May 1	May 9	June 17
NIDR	May 1	May 9	June 17
NIEHS	May 1	May 9	June 17
NIGMS	May 1	May 9	June 17
NINCDS	May 1	May 9	June 17
FIC	May 1	May 9	June 17
NLM	May 1	May 16	June 17
DRR	May 1	May 9	June 17

The review of evaluation projects will implement the recommendations in the Report of the Committee on the NIH Evaluation Program (March, 1984) and the Report of the Task Force on Evaluation Review Procedures. The NIH Evaluation Oversight and Policy Committee will perform concept review of all evaluation proposals that seek funding from NIH-wide evaluation set-aside funds. A technical review of proposals for all these proposals plus any BID proposals voluntarily submitted will be performed by a Technical Merit Review Committee. The final decision categories to be used in the technical merit review are "Recommended for Inclusion in the Evaluation Plan", "Not Recommended for Inclusion" or "Defer". The initial technical reviews will be completed by June 7. Proposals judged by the Review Committee "Not Recommended for Inclusion in the FY 86 Evaluation Plan" or "Deferred" may be revised and resubmitted to OADPPE by June 17. These resubmitted proposals will be reviewed by the Technical Merit Review Committee by June 25.

o ASPE/ASH review sessions with the NIH are expected to be held in July and August.

Preparation of the FY 85 Evaluation Plan

Conformity with format, style, and pagination standards provided by this guidance will expedite both the preparation of the Plan and its subsequent printing. A detachable guide for format and style standards is included (Attachment V).

Outline for BID Submissions.

- Proposed Budget. A table summarizing current activities, expenditures, and plans for future funding of all BID funded evaluation projects will be prepared according to the format provided in Attachment II. Projects for which set-aside funds are requested are to be submitted to the OD separately (leave project number blank - to be assigned by OD). Include in your Institute budget table:

  --Titles of all projects for which FY 1986 funds are requested.

  --Titles of all projects presently in process, whether or not additional funds will be required in FY 1986.

- Project Description and Justification Forms. Each BID is to provide completed forms for all new projects that are to be reviewed by the Technical Review Committee. While the draft ASPE guidance allows a mini-form for projects under $135,000, the full form is needed for NIH peer review of all projects. A copy of the form is included in Attachment III.

- Evaluation Documentation Center (EDC) Forms. Each BID is to provide completed forms for (1) all current projects and (2) all recently completed projects (completed since the FY 85 submission). See Attachment IV for the required content and format and a blank copy of the form. Instructions for completion of the form can be found in the User's Guide to the HHS Evaluation Documentation Center, Summer 1983, available from ASPE and from NIH/BID evaluation officers. It is also reproduced in Section VI-C of the Guide to the NIH Evaluation Program.

Presentation Order. Order the submission as follows:

- List of Projects and Proposed Budget

  Previously Approved Projects Deferred to FY 1986

  Projects in Process for which substantially increased funding is required (more than $25k)

  New Proposals $135k or More

  New Proposals Less Than $135k

  Evaluation Documentation Center Forms for Continuing and Recently Completed Projects

- o Project Description and Justification Forms

  --Order chronologically within section according to project number (for deferred projects, enclose a copy of the original PDJ, but show approved status in item 11 of that PDJ.)

  --Begin with the earliest proposal date.

  --For new projects, place forms for those mandated by the Congress or the Secretary first in the appropriate section.

- o EDC Forms

  --Order chronologically according to the year of initial proposal, beginning with the earliest proposal date.

Section Assignments. The chapter numbers to be used for the FY 1986 Plan are as follows:

1. Introduction
2. Summary List of Evaluation Projects and Budget
3. OD
4. NCI
5. NEI
6. NHLBI
7. NIA
8. NIADDK
9. NIAID
10. NICHD
11. NIDR
12. NIEHS
13. NIGMS
14. NINCDS
15. NLM
16. DRR
17. FIC

Appendix: Guidance for Preparation of FY 1986 Evaluation Plan

Numbers of Copies. Each BID will submit 15 copies of the Plan to Building 1, Room 228 or send 15 copies using form number 999 (3 hole punched 8 1/2 X 11 paper) to central printing at the DCRT Computer Center box 405.

Further Information. Contact the following at OD/PEB (Building 1, Room 228, telephone 496-4418):

- o Policy issues--Dr. Helen Gee
- o Guidance and review processes--Mr. Sheldon Fishman
- o Budgetary information--Ms. Cindy Peters
- o Preparation--Mrs. Sandy Cohen

Attachment I

Eligibility Criteria for the Use of Set-Aside Funds

To be eligible for support by evaluation set-aside funds, a project must be a part of the NIH-wide program and conform to one of the following descriptions:

1. Assessment of national health (research) programs funded by NIH:

   A wide range of program evaluation approaches can be included within this category. Projects with a narrow and external focus such as those designed to determine the effect of an Institute program on the state of knowledge in a particular scientific area obviously fits within this category, but so do those with a comprehensive and internal focus such as those with a comprehensive and internal focus such as those designed to appraise the entire programmatic structure of an Institute.

Program evaluations are expected to contribute information that will guide priority setting, resource allocation and other aspects of the planning process. While it is often difficult to distinguish between "planning" and "evaluation" in preparing a proposal, where a project has both a planning and an evaluation component a concentrated effort must be made to identify the evaluative component and estimate the associated costs that may be recovered from evaluation funds.

State of science assessments meet the set-aside criteria only if the assessments are clearly and explicitly related to program activities of an Institute and are part of an effort to evaluate program effects. Qualifying assessments generally involve time series analysis where baseline data are compared with data collected either at subsequent intervals or at the program conclusion.

Some suggested study topics in this category are:

- a. The relationship between the present research activities portfolio and currently perceived research opportunities,
- b. The appropriateness of present support mechanisms, and
- c. The possibilities for reallocation of funds.

It is important to note that set-aside funds may not be used to support:

- a. Studies undertaken only to determine or demonstrate the need for new programs
- b. Basic research, or
- c. Health services research.

2. Assessment of demonstration programs that have major implications for programs with national scope:

   Evaluations of demonstration programs may include assessments of effectiveness, cost, and public acceptance. Projects that attempt comparisons among demonstration programs with differing approaches to patient populations and projects to design methods for evaluating demonstrations are also permitted to be supported by set-aside funds. However, set-aside funds may not be used for the evaluation of a single demonstration project.

3. Assessment of program or program management processes procedures, intervention techniques, or information systems, except those specific to a single local project:

   Included herein are assessments of the efficiency, effectiveness, appropriateness, productivity, etc., of existing or alternative program support mechanisms (e.g., grants, contracts, centers, program projects, etc.). The development of techniques to be used by program staff to arrive at significant decisions concerning program direction or operation may also be the focus of a project within this category.

4. Evaluation of existing program policies to determine their impact on the activities of authorized programs:

   Included here are studies of the effects of alternative funding mechanisms on research production; the effects of specific Federal policies on researchers, institutions, or on research support programs themselves; the effectiveness of review procedures; the impact on society of the development of particular technologies, etc.

   This category does not include and set-aside funds are not available for the assessment of prospective policies for the development of new programs.

5. Design or development of general evaluation methodology as well as such methodology as may be developed for assessment of specific programs:

   The development and test of new techniques or approaches, to evaluation are eligible, e.g., development of methods to analyze scientific publications; development of methods to evaluate large, complex programs such as centers; development of techniques to assess review procedures, etc. Also eligible are assessments and analyses of program designs intended to produce more easily evaluated programs.

6. Initial design and development of management information systems for programs of national scope:

   Included here are projects such as the development of a program information system that provides access to an expansion of the IMPAC data base and the creation of a data base that will permit program activity to be tracked.

It is essential that the evaluative purpose of such information systems and data bases be clearly explained. There is a two year limit on the use of set-aside funds for projects within this category, after which the sponsoring unit is expected to use operating funds to continue the activity.

7. Initial development and pilot testing of instruments and procedures which, following development will be used for on-site project review and monitoring:

   This category does not include support for on-site reviews or monitoring activities.

8. Securing technical assistance to aid in the evaluation of eligible programs.

9. Short-term evaluation training of Federal employees whose professional concern is primarily evaluation of programs.

10. Addition of evaluation questions to a general purpose survey:

    Here the support of set-aside funds is only available for the incremental costs associated with the management and analysis of the evaluation questions. Proposed add-on projects will be reviewed according to the following criteria:

    (A) Evaluation is the primary purpose for the added questions; i.e., the questions would not be asked unless the evaluation were undertaken).

    (B) The information sought is essential to the evaluation of the program.

    (C) The desired information is not obtainable from other, more appropriate sources.

    (D) The proposed add-on survey is methodologically sound with regard to the goals of specific evaluation projects.

    (E) The information to be gained from the study is "worth" the dollar expenditure involved.

Examples of projects not eligible for "set-aside" funds

The following is an abbreviated list of some of the project types that are not eligible for set-aside funds.

1. Evaluation of a single project, center, etc.

2. Evaluation of an individual demonstration or experiment

3. Continued operation of management information or monitoring systems

4. Continued collection of baseline data.

5. On-site review and monitoring of local projects. The development and pilot testing of instruments is eligible for set-aside funding but the operation of onoing monitoring systems is not.

Attachment II

BID Evaluation Plan Current Program and Proposed Budget
(Format Instructions)

The format illustrated on the next page is to be followed by each BID in preparing the Summary of Projects and Budget. Please note the following points:

- o Where BID funds have been or will be used to support a project either in whole or in part, the amounts of set aside and BID funds should be listed separately with BID funds treated as a non-add item.
- o Projects should be listed chronologically by the fiscal year of initiation.
- o Where projects have only been conditionally approved, indicate this by appending the letter "c" after the amount.
- o Indicate by a footnote any projects involving any interagency agreements or co-funding.

SAMPLE FORMAT

National Heart, Lung, and Blood Institute: Proposed Budget

		$ in Thousands		
		FY 85	FY 86	FY 87
NHLBI 80-310	Assessment of Reach and Frequency of High Blood Pressure Messages	(50)	(45)	(45)
NHLBI 81-313	Evaluation of the Framingham and Otner CHD Risk Models in a Large National Cohort	--	--	--
NHLBI 84-407	Evaluation of Primary Reference Material Program	--	(40)	(30)
NHLBI 85-402	Assessment of the Role and Impact of Specialized Centers of Research (SCORs)	--	(200)c	--
	Total FY 86 NHLBI Evaluation Fund Request		(285)	

Notes

c - conditionally approved
( ) - non set-aside funds

Attachment III

NIH Evaluation Project Description and Justification Form -- FY 86 Format

1. NIH Evaluation Project Identifier: A unique identifier composed of the BID abbreviation, fiscal year of initiation, a code for the intended source of funding, and a 3 digit number assigned by the initiating BID that is unique within the BID for the fiscal year; e.g.

NHLBI 86 - 401 where	=	for projects supported solely by BID funds
NIH/NHBLI 86 - 301 where	=	for projects supported in whole or in part by set-aside funds. (These numbers will be assigned by OD)

2. Project Title and Capsule Description:

   a. Title: Short and descriptive

   b. Capsule Description: A one or two sentence characterization of the project.

3. Cost and Funding Source: For each of the fiscal years of planned project activity, list proposed expenditures of set-aside funds. Also include, enclosed in parentheses, planned expenditures of BID funds. In a parallel column list separately and DCRT (computer usage) charges. Please use the following format:

Fiscal Year	Total Expenditures (in thousands)	DCRT Charges (in thousands)	Other Expenditures (in thousands)
86	$20 ($5)	--	$20 ($5)
87	$40	--	$40
88	$20	$10	$10

Note: ( ) denotes BID funds.

(Provide a justification for the proposed level of effort, explaining--to the best of your ability at the present time--why the project should cost the estimated amount. To comply with consultant service requirements, please state why the project cannot be done in-house.)

4. Project Monitor/Contact: (name, office, address, and telephone number of the person responsible for developing work statement.)

5. Coordination: Identify the person(s) in your agency or other agencies who have reviewed the project. Please also name those individuals in other agencies who will have coordinative responsibility for the project.

6. Program Evaluated: Name and describe the program(s) being evaluated. Use the list of HHS program names that appears in the Summer 1983 edition of User's Guide to HHS Evaluation Documentation Center. Example: PHS-NIH-Biomedical Research - Intramural Research. In a few paragraphs describe what the program does, how big it is, and how it has evolved.

7. Intended User: State the intended user of the information to be generated and provide a timetable as to when the information generated by the study will be provided to the intended user.

8. Information to be Generated: Define the questions which will be answered through completion of the project; what will be known after the project is completed that is not now known. Please explain why it is important to acquire the information. Cite related work when appropriate.

9. Approach: Explain generally how the answers will be obtained; i.e., what data will be used, what comparisons will be made, will primary or secondary data be used. This section will be used by reviewers to determine whether a plausible approach for the project has been developed.

10. Information Clearance/Collection: Indicate with a Yes or No whetner or not the project involves data collection subject to OMB approval under the Paperwork Reduction Act of 1980.

Attachment IV

HHS Evaluation Documentation Center (EDC) Description Sheet
(FY 85 Format)

Project No.: (NIH Evaluation Project Number)

1. EDC ID No.: (Leave Blank)
2. Entry Dates: (Leave Blank)
3. Status: In Process or Complete
4. Project Title: (Short descriptive title of project - as approved)
5. Report Title: (Title(s) of final reports -- usually not yet determined for studies in process)
6. Agency Sponsor: (PHS-NIH-Institute Initials)
7. Start/End Dates: (Year and Month in the form 77-03, 80-01)
8. Performer: (Organization and address)
9. Agency Contact: (Name, NIH Building No., Room Number, Telephone No.)
10. Cost: (Cost by fiscal year(s) dollars in thousands in form FY 70-$45; FY 80-$30)
11. Fund Source: (Evaluation, S & E, etc.)
12. Mechanism: (Internal, Contract, etc.)
13. Project No.: (NIH Project No. - e.g. NCI 81-301)
14. Contract No.: (e.g. N01-OD-6-2149)
15. NTIS No.: (NYD or EDC Only)
16. ERIC No.: NA (Not Applicable)
17. Program(s) Evaluated: (According to the revised list of HHS program titles - see Attachment VI)

18. Evaluation Type: (Drawn from nine possible categories; See Guide to NIH Evaluation Program, Section VI.C, pg. 26)

19. Descriptors: (Selected from a fixed thesaurus of possible key words; See Guide to NIH Evaluation Program, SEction VI.C, pg. 67)

20. Abstract: The abstract should describe the essential features of the study in 250 words or less. It should be written so that a reader can decide whether or not to obtain the full report. The following points should be covered:

- The reason(s) for the evaluation and the purpose(s) it will serve,
- The expected findings,
- The analytic techniques to be used,
- The types of data collection involved,
- The target group or population,
- Any pertinent background information useful to a person who may not be an expert in the subject.
- Any special circumstances such as several agencies involved, a Congressionally mandated study, existence of related projects, etc.,
- The method of study dissemination, e.g., journal publication, agency report, etc. and
- The study results, conclusions, and recommendations (upon completion of study).

Blank Form for Drafting Entries of the Standard HHS Evaluation Study Description Sheet

1. EDC ID No.: Project No.:

2. Entry Dates: 3. Status:

4. Project Title:

5. Report Title:

6. Agency Sponsor: 7. Start/End Dates:

8. Performer:

9. Agency Contact:

10. Cost:

11. Fund Source: 12. Mechanism:

13. Project No.: 14. Contract No.:

15. NTIS No.: 16. ERIC No.: NA

17. Program(s) Evaluated:

18. Evaluation Type:

19. Descriptors:

20. Abstract:

Attachment V
Format and Style Requirements

Manuscript Preparation

Copy. Submit originals or excellent reproductions, appropriately centered on the page. These will be sent to the printer without retyping as "camera-ready" copy.

Page Format. Type on one side only, single spaced. Double space between paragraphs, which are indented five spaces. Leave one-inch margins at top, bottom, and sides. Begin on line 7 and end on line 60. The page may fall short of line 60, but may not run longer. Maximum line length is 6-1/2 inches (12 blank spaces at each end of line). Return to left margin after paragraph indent unless material is blocked, with bullets. Use Letter Gothic 12 type and 8-1/2" x 11" paper. (See Example B.)

Page Numbering. Number the page at the center of line 62, using assigned number as the first element of a two-part number (e.g., 4.1, 4.2). Begin numbering with Title/Contents page (4.1).

o Use odd numbers for the first page of each of the following sections:

--Budget summary

--Each project description and justification form

--Section comprising EDC forms

Headings. Capitalize the first letter of each word having four or more letters, as well as shorter, important words (e.g., Is, Are) and the second element of a compound word (e.g., Set-Aside). Center heads take precedence over side heads. Both should be underlined. Do not label heads with letters or numbers.

Sample Pages. See Example A for Title/Contents page. Do not include subordinate headings in the table of contents. For Summary and Proposed Budget page, see Example C.

Style Reminders

o Follow GPO Style Manual and Word Division; Webster's New Collegiate Dictionary.

o Spell out numbers through nine; use figures for 10 or more.

o One million, 10 million, but $1 million, $10 million.

o 1980s (no apostrophe).

o FY 1980, fiscal year 1980 (lower case). In tables only, use FY 80.

o Use comma before "and" and "or" in series (We saw John, Mary, and Bill).

o Capitalize Federal Government, Nation, Institute.

EXAMPLE A

4--line 11

NATIONAL CANCER INSTITUTE--line 13

Dr. Vincent T. DeVita, Jr., Director--line 15

Contents - line 18

List of Projects and Proposed Budget	4.3
Previously Approved Projects Deferred to FY 1986	4.x
Projects in Process for Which Substantially Increased Funding is Required (more than $25,000)	4.x
New Project Proposals $135,000 or more	4.x
New Project Proposals less than $135,000	4.x
Evaluation Documentation Center Forms for Continuing and Recently Completed Projects	4.x

4.1--line 62

EXAMPLE B

1--line 11

NAME OF INSTITUTE IN CAPS--line 13

This Is a Regular Center Head--line 16

line 18--This Is a Side Head

line 20-- This is a Run-In Head. It provides a third level of subordination. Note that it is indented five spaces, as are all paragraphs in regular text.

- o Bullets are indented five spaces. Skip one space between the bullet and the copy.
- o Note that the bullet text is block style.
  - --Further subordination in bullet copy is indicated by a dash (two hyphens), which is lined up with the preceding bullet copy.
  - --Leave no space between dash and text.
- o At the end of a bullet section, triple space before resuming text.

At the top of the second and subsequent pages, running text (or headline) starts on line 7. The copy runs to line 60 (or less, but never more).

The page number is centered on line 62 as shown below.

1.1·

18.18

DEPARTMENT OF HEALTH & HUMAN SERVICES

Korhse

Office of the Secretary

Memorandum

Date · FEB 27 1985

From Robert B. Helms Robert B. Helms
Acting Assistant Secretary for Planning and Evaluation

Subject FY 1986 Guidance for Evaluation Activities

To Assistant Secretary for Health
Assistant Secretary for Human Development Services

I am pleased to send you the FY 1986 Evaluation Guidance, which describes the procedures and schedule for development and approval of evaluation activities proposed for FY 1986.

As you know, in recent years we simplified the planning process and made changes intended to strengthen the capacity of OPDIV and agency evaluation offices to provide effective information services to program managers and policy makers. There are no major changes in the planning process for FY 1986, which again will consist of the following major elements:

- o Agencies will be required to submit a single plan to ASPE by August 15, 1985, consisting of a listing and description of continuing and new evaluation projects, and an evaluation budget covering the agency's needs for FY 1986.
- o ASPE will continue to delegate authority to the OPDIVs to approve all projects whose estimated cost over the duration of the project is $135,000 or less.
- o Additional evaluation projects which are submitted after the agency plans have been approved will be reviewed within ten working days after receipt by ASPE.

As I indicated to you in last year's Guidance, ASPE has initiated an effort to assess evaluation office operations and, in particular, their effectiveness in providing management and policy officials with high quality information within reasonable timetables. During this past year, we developed an assessment

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approach and pilot tested it within two PHS Agencies. When we have completed analyzing the results of this pilot study, we will share our findings and recommendations about the assessment approach with the OPDIVs and Agencies, as well as our plans for additional assessments of evaluation offices during Fiscal Years 1985 and 1986.

I look forward to working with you and your staff over the next few months in carrying out evaluation planning for FY 1986. If your staff have any questions, they may contact Tom Hertz of our Division of Evaluation (HHH 436 G6, 245-7181) for assistance.

Attachment

GUIDANCE FOR HHS EVALUATION ACTIVITIES IN FY 1986

prepared by

The Office of the Assistant Secretary
for Planning and Evaluation

For information contact:

Division of Evaluation
Office of Evaluation and Technical Analysis
Office of the Assistant Secretary
for Planning and Evaluation

HHH 436 G 245-7181

18.21

FY 1986 Highlights

● No major changes in the planning process for FY 86	For FY 1986, Agencies again will be required to submit a single plan to ASPE by August 15, 1985, consisting primarily of a listing and description of continuing and proposed evaluation projects. A schedule of major events in the planning process is presented on pp. 3-4, and the required content of the plan is described on p. 5.
● Delegation of authority for projects $135,000 or less	ASPE will continue to delegate authority to the OPDIV for all projects with an estimated cost of $135,000 or less. At the discretion of the OPDIV head, the approval authority may be further delegated to an Agency head. A mini-description of each of these projects should be included in the plan, as explained on p. 6.
● ASPE continues to encourage short-term policy oriented evaluation studies	Over the last several years, the Department has achieved a better balance between long and short-term studies. A number of agencies have established contracting mechanisms which facilitate short-term efforts, such as Delivery Order Contracts or Basic Ordering Agreements. ASPE is willing to assist evaluation offices in developing this capability.

● ASPE encourages evaluation offices to be responsive to the information needs of managers and policy makers.	We expect evaluation offices to try to shape evaluation projects through interaction between line management/ policy officials and evaluators. During 1984, ASPE pilot tested an approach to assessing the overall effectiveness of evaluation offices, including the extent of their success at providing policy officials and management with timely, useful information. ASPE's assessment effort is described on p. 7.
● Guidelines for using one-percent set-aside funding are generally unchanged.	Criteria for eligibility for "1% set-aside" funding are contained in Appendix I. There are ten categories of projects clearly eligible for set-aside funds. In general, these funds cannot be used for activities normally associated with the on-going operations of a specific program.

Schedule of Major Events in Planning Process

April to June	>>>--------->	**AGENCIES DEVELOP PLANS** Each Agency should begin to develop FY 1986 plans after meetings with the Agency head and program managers.
June 1 to July 30	>>>--------->	**AGREE ON DEPARTMENTAL INFORMATION AGENDA** The Assistant Secretary for Planning and Evaluation will meet with OPDIV and Agency heads to define major issues on which information is to be generated for the Office of the Secretary and OPDIV. The status of information developed in response to last year's issues will serve as the basis for the FY 1986 discussions. Participants also may present major studies begun last year.
July 15	>>>--------->	**EVALUATION PLANS SUBMITTED TO OPDIV** All Agency evaluation plans should be submitted to the OPDIV head by July 15, 1985.
August 15	>>>--------->	**EVALUATION PLANS SUBMITTED TO ASPE** OPDIVs will review all Agency projects and forward the approved plan to ASPE by August 15th, 1985.

August 15 to
September 15 >>>--------->

ASPE RESPONDS TO OPDIV AND AGENCY

After plans are submitted and reviewed, ASPE will submit the results of its review by memorandum to the OPDIV. If necessary, ASPE will meet with the OPDIV and Agency to obtain agreement on the projects submitted in the Agency plan. At these meetings, Agency, OPDIV and ASPE staff will resolve questions regarding projects. ASPE will issue a memorandum summarizing the agreements reached at the meetings within two weeks. Agency budgets will be established, based on the total estimated costs of those projects approved as of October 1. These budgets can be revised as necessary during the fiscal year, as additional projects are approved.

Ongoing >>>---------->

AGENCY PLAN AMENDMENTS

Throughout FY 1986, agencies may submit additional projects, or otherwise amend their plans to reflect new information needs of Agency heads and program managers. Each Agency evaluation office should have a systematic process to identify these information needs. ASPE will review amendments within ten working days.

EACH AGENCY FY 86
EVALUATION PLAN
SHOULD INCLUDE:

TOTAL PROPOSED BUDGET:	Total amount required to fund all evaluation projects in FY 86.
CONTINUING PROJECTS:	List of titles and FY 86 costs.
NEW PROJECTS OVER $135,000:	List of titles, full project descriptions, and estimated costs.
NEW PROJECTS $135,000 AND UNDER:	List of titles, mini-project descriptions, and estimated costs.
UNANTICIPATED PROJECTS > $135,000:	Dollar estimate, to be set aside, for projects to be developed throughout the year (optional).
UNANTICIPATED PROJECTS < $135,000:	Dollar estimate, to be set aside, for projects to be developed throughout the year (optional).

Procedures for Submitting Plan

ALL PLANS SHOULD BE SUBMITTED TO ASPE THROUGH THE OPDIV HEAD.

This will assure that the plans reflect the OPDIV's information needs and that the OPDIV concurs with the evaluation budget request of the Agency.

PROJECTS OVER $135,000 MUST BE APPROVED BY THE ASSISTANT SECRETARY FOR PLANNING AND EVALUATION.

Standard project description and justification (PDJ) forms should be used to propose these projects in the plan. (See Appendix II for PDJ format.)

To encourage a quick response capability throughout the year, project descriptions (or RFPs, if they have been requested) submitted by agencies to ASPE after the initial plan submission will be reviewed within ten working days after receipt by ASPE of the approval request from the OPDIV head.

FOR FY 1986, THE ASSISTANT SECRETARY FOR PLANNING AND EVALUATION DELEGATES APPROVAL AUTHORITY TO THE OPDIV HEAD FOR ALL PROJECTS $135,000 AND UNDER.

The objective of this delegation of authority is to assure relevance and timeliness of the information made available to OPDIV and Agency heads.

For these projects, mini-descriptions (see Appendix IIB) should be submitted for information purposes in the plan, and throughout the year as new projects are developed. While approval of these projects has been delegated to the OPDIV head, ASPE will advise the OPDIV if there is an obvious case of duplication or non-conformity to departmental procedures or policies. ASPE also may be interested in receiving briefings on the results from selected evaluations.

ASPE Evaluation Assessments

THE FY 1984 EVALUATION GUIDANCE ANNOUNCED ASPE'S INTENTION TO CONDUCT ASSESSMENTS OF HHS AGENCY EVALUATION OFFICES.

The primary purpose of these assessments is to examine evaluation office's overall capability, including the extent to which they are successful at providing their management and policy officials with high quality useful information within reasonable timetables. It is hoped that the assessment process will enhance communication between line managers and evaluation offices.

The assessments also examine the impact of the delegation of authority for projects under $135,000. The delegation was intended to help OPDIV and Agency evaluation offices provide more effective information services to program managers and policy makers.

Another objective of the assessments is to identify examples of excellence in evaluation planning, study design and execution, and information dissemination, and encourage replication of the good practices in other parts of the Department.

AN ASSESSMENT APPROACH WAS DEVELOPED AND PILOT TESTED IN TWO PHS AGENCIES DURING 1984. ASPE PLANS TO CONDUCT ADDITIONAL ASSESSMENTS DURING 1985.

The results of the pilot effort are now being analyzed by ASPE. Findings and recommendations about the assessment approach will be shared with OPDIVs and Agencies, and will be used to develop a plan for additional assessments of evaluation offices during Fiscal Years 1985 and 1986.

APPENDIX I

EVALUATION PROJECTS ELIGIBLE FOR "SET-ASIDE" FUNDS

For a number of years, the Department has defined evaluation as follows:

> Evaluation is the measurement of program performance (efficiency, effectiveness, responsiveness), the making of comparisons based on those measurements, and use of the resulting information in policy-making and program management.

Questions frequently arise, however, regarding the criteria that govern the types of evaluation projects eligible for evaluation "set-aside" funds. The term "set-aside" refers to programs with authorizing legislation that permit program funds to be used for evaluation of the Public Health Service and some programs in the Office of Human Development Services. No set-aside funds are authorized for programs in the Food and Drug Administration, the Social Security Administration, and the Health Care Financing Administration.

In reviewing a project's eligibility for set-aside funding, the following criteria (not listed in priority order) will be used:

1. Evaluation of HHS funded national programs.
2. Evaluation of demonstration programs which have major implications for design or redesign of national programs. (Evaluation of research and development "demonstrations" are generally not eligible for set-aside funding.)
3. Evaluation of program or program management processes, procedures, intervention techniques, or information systems, except those specific to a single local project.
4. Evaluation of existing policies to determine their impact on program activities or currently authorized programs. (The assessment of prospective policies, where no programs yet exist, is not eligible for set-aside funds.)
5. The design and development of general evaluation methods and methodology developed for the assessment of specific programs. Support for the development of methodologies to assess individual projects is appropriate, and may include preparation of project evaluation manuals or handbooks

for grantees. (The execution of these methodologies to evaluate individual local projects is not eligible for set-aside funding.)

6. The initial design and development of management information systems and other data systems whose primary purposes are to evaluate programs of national scope. The use of evaluation funds to finance the design and development of these systems is limited to two years, starting from the design phase. After two years, agencies are expected to support systems from operating funds.

7. Initial development and pilot testing of instruments and procedures which will be used for on-site project review and monitoring. While initial development and pilot testing are eligible for evaluation support, agencies are expected to fund ongoing monitoring systems from program funds.

8. Securing technical assistance to help with the evaluation of eligible programs, excluding assistance to a single local project.

9. Short-term evaluation training of Federal employees whose professional concern is primarily evaluation of programs. Evaluation training for state and local officials is not eligible for "set-aside" funding.

10. The addition of evaluation questions to an on-going general purpose survey. However, the cost to be incurred by evaluation funds is limited to the marginal cost of adding the questions and analyzing the evaluation data. Proposed add-on projects will be reviewed according to the following criteria:

    (A) Evaluation is the primary purpose for the added questions, (i.e., the questions would not be asked unless the evaluation were undertaken).

    (B) The information sought is essential to the evaluation of the program.

    (C) The desired information is not obtainable from other, more appropriate, sources.

    (D) The proposed add-on survey is methodologically sound with regard to the goals of specific evaluation projects.

    (E) The information to be gained from the study is "worth" the dollar expenditure involved.

Examples of projects not eligible for "set-aside" funds

As a general rule, the following types of projects are not eligible for "set-aside" funding:

1. The evaluation of individual local projects.
2. The evaluation of individual "R&D" experiments and demonstration projects.
3. The continuing operation of management information systems or ongoing monitoring systems. As noted in #6 above, the use of evaluation funds to finance the design and development of management information systems is to be limited to a maximum of two years.
4. The continuing collection of baseline data.
5. On-site review and monitoring of local projects. The development and pilot testing of instruments and procedures for on-site project review and monitoring is eligible for set-aside funding (as noted in #7 above) but the operation of ongoing monitoring systems is not.

APPENDIX II

PROJECT DESCRIPTIONS

A. Standard Project Description and Justification -- Projects over $135,000

A standard Project Description and Justification (PDJ) form is required in the evaluation plan for every evaluation project over $135,000, whether in-house or contract. The PDJ covers not only the important elements of evaluation project planning, but also the information required by the current GAM Chapter 8-15 on consultant services policies and procedures. Also, note the new requirement for information on prerulemaking activity.

The PDJ is expected to provide the basis for a more detailed "work statement" required for procurement or in-house projects, and serves as a "contract" between the evaluation unit and the specific audience requesting the study. Project descriptions should not be submitted to ASPE until both the evaluation unit and the officials who will use the study are satisfied with its content.

PDJs should conform to the following format:

1. Project ID # and Agency Proposing: Provide a unique, centrally-assigned identifying number showing Agency or OS staff office, fiscal year of initiation, and a three-digit number, e.g., ADAMHA-82-001, ADAMHA-82-002, etc.

2. Project Title: Title and a one-to-two sentence description of the project.

3. Cost and Funding Source: Estimated cost for prior, current, and following fiscal year and each appropriation to be used. Please note if study is a continuation.

   Provide a justification for the proposed level of effort, explaining the cost estimate. To comply with consultant service requirements, please state why the project cannot be done in-house.

4. Project Monitor/Contact: Name, office, address, and telephone number of the person responsible for developing work statement.

5. Coordination: Identify the person(s) in your Agency or other agencies who have reviewed the project. Please also name those individuals in other agencies who will have coordinative responsibility for the project.

6. Program Evaluated: Name the program(s) being evaluated, including the major program element(s) or subprogram.

7. Intended User: State the intended user of the information to be generated and provide a timetable as to when the information will be available.

8. Information to be Generated: Define the questions which will be answered through completion of the project; what will be known after the project is completed that is not now known. Please explain why it is important to acquire the information. Cite related work when appropriate.

9. Approach: Explain generally how the answers will be obtained; i.e., what data will be collected, what comparisons will be made, will primary or secondary data be used.

10. Information Clearance/Collection: Indicate with a yes or no whether or not the project involves data collection subject to OMB approval under the Paperwork Reduction Act of 1980.

11. Prerulemaking Activity: Indicate whether or not the project involves prerulemaking activity, i.e., has the potential for resulting in the development of significant regulations or guidelines, as defined in Executive Order 12498 and OMB Bulletin 85-9.

B. Mini-Description — Projects $135,000 and Under.

For projects $135,000 and under, mini-descriptions (one to two pages) should conform to the following format:

1. Project ID # and Title

2. Information to be Generated: Summarize what is going to be learned from the project.

3. Intended Use: Summarize why the Agency desires the information to be gained from the project.

4. Cost and Timing: Indicate the estimated cost and when the information will be made available.

5. OMB Review: Indicate with a yes or no whether or not this project includes data collection subject to OMB approval under the Paperwork Reduction Act of 1980. Also indicate whether or not the project involves prerulemaking activity, i.e., has the potential for resulting in the development of significant regulations or guidelines, as defined in Executive Order 12498 and OMB Bulletin 85-9.

APPENDIX III

SUBMISSIONS TO THE EVALUATION DOCUMENTATION CENTER

Within ASPE, the Evaluation Documentation Center (EDC) tracks, compiles and retrieves information on HHS evaluations, publishes the Compendium of HHS Evaluation Studies, and offers specialized searches of its data base.

Users with access to ADABAS in the Parklawn Center can query the EDC data base through an on-line system. The on-line data base is accessible through program name, type of evaluation, e.g. impact, or subject.

In order to keep this information up-to-date, the following materials should be submitted to EDC for each evaluation:

- the one-page HHS Evaluation Description Sheet (see attached form) at the time of project initiation, and a revised description sheet upon major change in status, including completion of the study;
- three copies of the final evaluation report;
- an executive summary of the final evaluation report;
- an NTIS bibliographic data sheet (see attached form).

In preparing the scope of work for an evaluation contract, the Agency may want to include completion of the HHS Evaluation Description Sheet and the NTIS bibliographic data sheet as a task to be performed by the contractor.

****

For more detailed instructions on submitting evaluation information to the EDC or querying the EDC data base, phone 245-6445.

STANDARD HHS EVALUATION STUDY DESCRIPTION SHEET

1. EDC ID No.:

2. Entry Dates:

3. Status:

4. Project Title:

5. Final Report Title:

6. Agency Sponsor:

7. Start/End Dates:

8. Performer:

9. Agency Contact:

10. Cost: FY -$,FY -$,FY -$,FY -$,FY -$

11. Fund Source:

12. Mechanism:

13. Project No.:

14. Contract/Grant No.:

15. NTIS No.:

16. ERIC No.:

17. Program(s) Evaluated:

18. Evaluation Type:

19. Descriptors:

20. Abstract:

NTIS BIBLIOGRAPHIC DATA SHEET

50272-101

REPORT DOCUMENTATION PAGE

1. REPORT NO.

2.

3. Recipient's Accession No.

4. Title and Subtitle

5. Report Date

6.

7. Author(s)

8. Performing Organization Rept. No.

9. Performing Organization Name and Address

10. Project/Task/Work Unit No.

11. Contract(C) or Grant(G) No.

(C)

(G)

12. Sponsoring Organization Name and Address

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement

19. Security Class (This Report)

21. No. of Pages

20. Security Class (This Page)

22. Price

(See ANSI–Z39.18)

See Instructions on Reverse

OPTIONAL FORM 272 (4–77)
(Formerly NTIS–35)

MINUTES
NIH Evaluation Policy and Oversight Committee
May 17, 1985

Members: Present:	Mr. Kurt Habel (Chairman, OD), Drs. Ruth Kirschstein (NIGMS), Mortimer Lipsett (NIADDK) and Mr. Sheldon Fishman (Exec. Secretary, OD). Drs. Robert Gordon (OD) and Harald Loe (NIDR) submitted written comments. Drs. Philip Chen (OD) and Claude Lenfant (NHLBI) were unable to attend.
Observers:	Drs. Helen Gee (OD) and Charles Lowe (NICHD)

The committee met to review 11 proposed evaluation studies, to review a proposal to submit an unsolicited proposal on evaluation of clinical studies and to determine the size of the set-aside budget for FY 1986.

Concept Review

Project	Recommendation
NIH/NICHD 85-312 NICHD Intramural Research Matched Comparison Evaluation Using Citation Analysis Within Co-Citation Clusters	Include

When an earlier draft of this project was reviewed (see Minutes of 3/27/85), the Committee deferred making a recommendation. Dr. Charles Lowe was asked to address several questions and to provide an oral presentation. This project will develop new bibliometric methodologies to evaluate intramural programs. These methods will locate publications within biomedical clusters and develop aggregate quality measures based on citations. The methodology will be tested on the NICHD intramural program as requested by the current NICHD Board of Scientific Counselors. The Committee approved this project for set-aside funds because if it is successful other BID Boards of Scientific Counselors may request similar information.

NIH/CC 85-314 Feasibility Assessment for a Study of Patient Classification System Alternatives in the NIH Clinical Center	Include

This project will evaluate the current patient classification system utilized by the clinical center for determining nursing staffing for each shift ("nursing productivity"). The Committee approved this project for funding in FY 1985.

Project	Recommendation
NIH/DRG 85-315 Improvement of Information About Earned Degrees of Grant Applicants This project will correct the information in the IMPAC database on the academic degree earned by NIH grant applicants. The Committee approved this project for funding in FY 1985.	Include
NIH 86-301 Development of an Inventory of Data Elements in Existing Databases That are Useful for Program Evaluation This project will develop a data dictionary of information elements that are useful for program evaluation and now exist in computer databases.	Include
NIH 86-302 Evaluation of the Applicability of Biomedical Expert Systems for the Improved Management of Biomedical Research This project will pilot test the applicability of expert system techniques to improve the productivity of research administration and support.	Include
NIH/DRR 86-307 Evaluation of NIH Shared Research Instrumentation Activities This project responds directly to questions asked by the Office of the Assistant Secretary of Health and the Office of the Secretary on shared instrumentation. The project is proposed by two BIDs and has NIH-wide applicability.	Include
NIH/NLM 86-305 Development of Evaluation Methodologies to Assess NLM's Coverage of New Biomedical Literature This project will develop methodologies to assess the scope of NLM's coverage and access to that literature in new biomedical fields.	Include

Project	Recommendation
NIH/NLM 86-306 Evaluation of the Scope and Coverage of NLM's TOXLINE Database This project will evaluate the scope and coverage of the NLM's Toxicology Literature Online (TOXLINE) file. The Committee had a question about the applicability of this project to other BIDs. The Committee would like a revised proposal that includes the view of BID users of TOXLINE (e.g. Dr. David Rall (NIEHS) and NCI).	Deferred
NIH/FIC 86-308 Development of a Model System for the Collection and Analysis of Data on Expenditures for Biomedical Research by Major Countries This project will develop a system for the collection and analysis of national expenditures for biomedical research by major countries. The committee was skeptical about NIH's ability to develop common definitions for expenditures that will be adopted by other countries. Further effort in this direction should be delayed until the current OECD detailed effort is completed.	Not Included
Letter requesting permission to submit an unsolicited proposal for the Evaluation of Clinical Trials The suggested proposal would analyze quality scores and patterns of citations for randomized clinical trials. The committee believes that this realm of research may more appropriately be supported by a research grant.	Not Included
NIH/DRS 86-303 Productivity Evaluation of the Biomedical Engineering and Instrumentation Branch (See below)	Deferred

Project	Recommendation
NIH/DRS 86-304 Productivity Evaluation of the Division of Research Services	Deferred

These two projects will analyze the productivity of programs within DRS. Because of the overlap between the projects, the Committee requests a revised project which consolidates both projects and highlights the need for this project, given the widely-recognized quality and effectiveness of DRS activities.

Project	Recommendation
NIH/NIDR 86-309 Assessment of NIH, Industry, and Academic Relationships in Restorative Materials Research	Deferred

This project will analyze the relationsips among government, industry and academe in restorative dental materials research. The committee has questions about the inclusion of this project in the NIH-wide set-aside program:

- Are other BIDs interested in participating in this study?
- How would the results be applicable to other BIDs?
- What is the basis for the cost of this project, $250,000?
- What will this project add to the information NIH is already receiving as a participant in the NAS Government-University-Industry Research Roundtable?

Project	Recommendation
NIH/NIDR 86-310 Bibliometric Evaluation of Social and Behavioral Science Research in Dentistry	Deferred

This project will analyze social and behavioral science research in dentistry. The Committee questions how the results of this project will be applicable to other BIDs. In addition, the project should be deferred until after the special BID Directors meeting on May 31 and possibly revised to reflect any appropriate concerns about behavioral research that may emanate from that meeting.

Budget

The committee reviewed the budget analysis prepared by OPPF and determined that the size of the set-aside evaluation budget for FY 1986 would be $3 million. If the total projects approved by the Committee by the end of the third quarter of FY 86 project expenditures of a lesser amount, remaining funds will be returned to the BIDs.

Prepared by Sheldon Fishman

Minutes
NIH Evaluation Policy and Oversight Committee
July 30, 1985

Members: Present: Mr. Kurt Habel (Chairman, OD), Drs. Philip Chen (OD), Ruth Kirschstein (NIGMS), Harald Loe (NIDR), and Mr. Sheldon Fishman (Executive Secretary, OD). Drs. Robert Gordon (OD), Claude Lenfant (NHLBI), and Mortimer Lipsett (NIADDK) were unable to attend.

The Committee met to review a proposed evaluation of research opportunities in biology and four proposals which were revised since their deferral by the Committee on May 17, 1985.

Project	Recommendation
NIH-85-316	
Evaluation of Research Opportunities in Biology	Include

The National Academy of Science will establish panels of experts to identify scientific opportunities in biology and will recommend action to seize these opportunities. The National Science Foundation and Department of Agriculture have already approved and committed funds for this study. The Committee approved this project because it should provide useful information for program management.

NIH/DRS 86-304	
Productivity Evaluation	Include

DRS had submitted two proposals, one to evaluate productivity of the Biomedical Engineering and Instrumentation Branch and the other to conduct "Productivity Evaluations" of several other branches of the Division of Research Services. In May, the Committee deferred both projects because:

> "These two projects will analyze the productivity of programs within DRS. Because of the overlap between the projects, the Committee requests a revised project which consolidates both projects and highlights the need for this project, given widely-recognized quality and effectiveness of DRS activities."

DRS submitted a revised proposal which consolidates and integrates the projects in a phased set of studies over three years. In addittion, Dr. Whitney's cover memo highlights the need for this project: "by the end of FY 1987, DRS is committed to operating its programs with a decrease in personnel of 12 percent from the FY 1984 FTE ceiling" and "increases in user charges to be implemented in FY 1986 will have a dramatic impact". The Committee approved the project but was concerned with the high cost of the effort and expects the DRS to assess carefully the total costs of this project once phase I experience has been gained and to submit a revised budget estimate at that time.

Project	Recommendation
NIH/NIDR 86-309	
Assessmenmt of NIH, Industry, and Academic Relationships in Restorative Materials Research	Include

In May, the Committee deferred this project because of its focus on a single research area. Several questions were raised:

- o Are other BIDs interested in participating in this study?
- o How would the results be applicable to other BIDs?
- o What is the basis for the cost of this project, $250,000?
- o What will this project add to the information NIH is already receiving as a participant in the NAS Government-University-Industry Research Roundtable?

NIDR submitted a revised proposal and two memos: Dr. Loe's cover memo and a memo from Julian Morris which express NEI interest in the end product and the methodology of the study. Dr. Loe distinguishes between the empirical information to be provided by this study and the discussions of broad policies considered by the NAS Government-Industry Research Roundtable. The Committee approved this study but expects the total costs of the project to be assessed carefully to determine if the study costs can be reduced.

NIH/NIDR 86-310	
Bibliometric Evaluation of Social and Behavioral Science Research in Dentistry	Include

In May, the Committee deferred this project because: "This project will analyze social and behavioral science research in dentistry. The Committee questions how the results of this project will be applicable to other BIDs. In addition, the project should be deferred until after the special BID Directors meeting on May 31 and possibly revised to reflect any appropriate concerns about behavioral research that may emanate from that meeting."

NIDR submitted a revised proposal and a memo from the Chairperson of the NIH Health and Behavior Working Group which states that this project "will be broadly useful to Social and Behavioral Science programs throughout the NIH". The Committee approved this project to test the feasibility of applying bibliometric techniques in this area.

Project	Recommendation
NIH/NLM 86-306	
Evaluation of the Scope and Coverage of NLM's TOXLINE Databases	Include

In May, the Committee deferred this project because: "The Committee had a question about the applicability of this project to other BIDs. The Committee would like a revised proposal that includes the view of BID users of TOXLINE (e.g. Dr. David Rall (NIEHS) and NCI)."

NLM revised its proposal and advised the Committee that the Toxicology Information Subcommittee of the DHHS Committee to Coordinate Environmental and Related Programs were strongly in favor of the proposed study. That subcommittee includes a representative from NIEHS. The NIH Evaluation Committee approved this study.

Prepared by Sheldon Fishman
(496-4418)

Minutes
NIH Evaluation Policy and Oversight Committee
September 17, 1985

Members: Mr. Kurt Habel (Chairman, OD), Drs. Phillip Chen (OD), Ruth Kirschstein (NIGMS), Claude Lenfant (NHLBI), and Mr. Sheldon Fishman (Executive Secretary, OD). Drs. Mortimer Lipsett (NIADDK) and Harald Loe (NIDR) were unable to attend, but Dr. Loe's written comments on each page were discussed.

Observers: Drs. Jerome Yates (NCI) and Helen Gee (OD)

The Committee met to review three new proposed evaluations and a proposal which was revised since its deferral by the Committee on May 17, 1985.

Project	Recommendation
NIH/NCI 86-312	
Request for Add-on Funds for the Hospital Cost and Clinical Research Project	Include

The Hospital and Clinical Research Project (HCCRP) is a collaborative study being conducted by NIH and the National Center for Health Services Research (NCHSR). It is currently supported by 1% set-aside funds from the Office of the Assistant Secretary for Health at $516,000 over two years. The study is designed to examine the effects of Medicare's prospective payment system (PPS) on cancer clinical research by examining the costs of providing hospital care for patients on clinical trials and studying changes in patterns of treatment for cancer patients before and after PPS.

The proposed project would add $190,000 to perform tasks that were not anticipated in the original plan. The Committee recognized the critical need for information relevant to clinical trials. Despite reservations about the applicability of findings from cancer clinical trials to clinical trials supported by other BIDs, the Committee approved this project because it is important and timely and because it is clearly of interest throughout other components of DHHS.

NIH/FIC 86-308	
Development of a Model system for the Collection and Analysis of Data Expenditures for Biomedical Research by Major Countries	Not Include

The Committee recommended not to include this project when it was reviewed on May 17 because "the Committee was skeptical about NIH's ability to develop common definitions for expenditures that will be adopted by other countries. Further effort in this direction should be delayed until the current OECD detailed effort is complete."

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Dr. Farlee's memo identifies the approach that will be used to implement the model system and outlines the differences between the proposed study and related studies. The Committee remains unconvinced that the product of this feasibility study (a prototype data collection system) will be successfully implemented or supported on a continuing basis by a number of developed countries. In addition, experience with U.S. data reveals that these data are very hard to obtain and of limited accuracy. For international comparisons, the problem of accuracy is likely to be exacerbated substantially; some countries have many different sources of support for biomedical research and international comparisons add the complexity of different currencies. Finally, the Comittee felt that the utility of these data was limited; while some additional analyses may be useful, the overall conclusions are already well known and these data are not useful for planning or resource allocation at NIH.

NIH 75-1

National Academy of Sciences Continuing Study of National Needs for Biomedical and Behavioral Research Personnel	Include

These assessments of training programs and projections of manpower needs for biomedical and behavioral researchers are mandated by Congress and have often been useful to NIH. The Committee recognizes that the annual cost of these studies has been reduced and considerable effort has been made to increase the utility of the studies. The Committee approved this project but hopes that the actual costs will be less than the current estimated budget.

NIH/NIADDK 86-301

Survey of Physician Practice Behaviors Related to the Treatment of People with Diabetes Mellitus	Not Include

This survey will provide data concerning current practice in treating diabetes. The results of this study will be used to direct educational efforts and to provide baseline data for assessing change over time (e.g. after a NIH Consensus Development conference). The Committee noted that the value of studies of physician practices before and after a major intervention has been demonstrated several times. Interest in this type of study is likely to grow as a result of an evaluation of the NIH Consensus Development program which will be released in a few months. However, the Committee decided to recommend not including this study in the NIH-wide program because the results of the particular study are applicable almost exclusively to NIADDK.

Prepared by
Sheldon Fishman, OPPE

APPENDIX 6

FEDERAL POLICY FOR BIOMEDICAL AND BEHAVIORAL RESEARCH

Adopted by the Executive Council of the
Association of American Medical Colleges
April 10, 1986

AAMC ad hoc Committee on Federal Research Policy

EDWARD N. BRANDT, Jr., M.D., *Chairman*, Chancellor, University of Maryland at Baltimore

STUART BONDURANT, M.D., Dean, University of North Carolina at Chapel Hill School of Medicine

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ELIZABETH M. SHORT, M.D., Director, Division of Biomedical Research and Faculty Development, Association of American Medical Colleges

DAVID B. MOORE, Staff Associate, Division of Biomedical Research and Faculty Development, Association of American Medical Colleges

PREAMBLE

The federal government's commitment to improving the health and well-being of the American people incorporates a wide spectrum of programs and initiatives. An essential portion of this commitment is the system of biomedical and behavioral sciences research that has evolved as a result of the continued investment of federal funding. The success of this federal biomedical research enterprise in terms of scientific achievement and societal benefit is a testament to the policies that have guided this program over the last 40 years.

The recent pressure for deficit reduction on the Congress and the administration will force a reassessment of a number of these research policies. There is concern within the academic medical community that in their efforts to achieve a fiscally responsible budget, policy makers are concentrating on the short-term economic perspective rather than the longer-term programmatic consequences of reductions in research budgets.

An additional stimulus for reexamination of the Association's positions on federal research policy was provided by the House of Representatives Science Policy Task Force, chaired by Representative Don Fuqua (D-FL). This Task Force is conducting a 2 year study of all aspects of national science policy. The Association is concerned to assure that the Task Force receives thoughtful analysis of policy from all segments of the scientific community and that those elements of federal research policy that uniquely contribute to the preeminence of American biomedical and behavioral research be especially clearly articulated before a Task Force whose parent Committee on Science and Technology does not regularly deal with the Public Health Service research agencies.

As a result, the Association of American Medical Colleges appointed an *ad hoc* Committee on Federal Research Policy in June 1985. The Committee was given the general charge to conduct an overview of those broad policy issues related to the federal role in biomedical and behavioral sciences research as currently being debated by the Congress and the administration. The Committee was to develop new positions or reaffirm existing Association positions as the basis for its recommendations in six key areas related to biomedical and behavioral sciences research:

- goals of the federal research effort
- research manpower and training
- research infrastructure
- research awards system
- federal funding for research
- formulation of federal science policy

The following report contains the analysis and recommendations of the Committee. It is hoped that this report will facilitate the Association's participation in the public debate engendered by this crucial set of issues.

EXECUTIVE SUMMARY

Biomedical and behavioral sciences research in the United States is conducted predominantly within our nation's medical schools and academic medical centers, where the academic faculty seek to contribute new knowledge, educate the next generation of health professionals, and provide cutting edge patient care. The major source of support for biomedical and behavioral research comes from federal investment. In 1984, 58 percent of the National Institutes of Health (NIH) extramural budget was spent in academic medical centers and 67 percent of National Research Service Awards funds from NIH were awarded for research training in the health professions to academic medical centers or their trainees.

Thus, the Association of American Medical Colleges, which represents the nation's 127 medical schools, over 450 of its teaching hospitals, and over 80 academic faculty societies, is vitally concerned with the programs and policies that govern the federal investment in biomedical and behavioral sciences research. The Association's *ad hoc* Committee on Federal Research Policy has recently completed an analysis of present policy in key areas of the research effort and offers the following recommendations in response to the current pressures to reexamine the policy basis of the national research effort and establish funding priorities.

I. THE GOAL OF THE FEDERAL EFFORT IN BIOMEDICAL AND BEHAVIORAL SCIENCES RESEARCH

The goal of federally supported biomedical and behavioral sciences research should be to acquire an expanded base of scientific knowledge to improve the health of the American people. The federal commitment to this goal is reflected in the long-standing investment in biomedical research, which has resulted in the evolution of the world's preeminent bioscience enterprise.

Health research is conducted and supported by a number of federal departments and agencies; however, only the NIH and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) have the acquisition of basic biological and clinical knowledge as their primary mission. This mission must be protected and enhanced. Other vital and necessary components of national health policy, such as public education, demonstration projects, and health care delivery, should be entrusted to other agencies within the Public Health Service (PHS), other federal agencies, or, where appropriate, the private sector. In addition, the obligations of the NIH and ADAMHA need not be extended to include full responsibility for the translation of basic biological and clinical knowledge to patient care. Finally, the goal of biomedical research must be realized through pursuit of excellence in research. The limited resources available for fundamental research must not be deployed to achieve non-scientific objectives. The benefit to all aspects of the economy derived from research should be a consequence, not a goal of the research effort.

II. THE SCALE AND SCOPE OF THE FEDERAL INVESTMENT IN BIOMEDICAL AND BEHAVIORAL SCIENCES RESEARCH

The federal contribution to biomedical research through the NIH and ADAMHA is unique because it emphasizes basic biological and clinical investigations, many of which would go unfunded without federal support. In fact, the overall biomedical research enterprise that has evolved as a result of this federal investment is of such a scale that only continued federal support can sustain it.

Biomedical research is a long-term endeavor; the nation's medical schools and academic medical centers took years to develop the talent and resources necessary to achieve the current level of productivity. Reductions in federal support for biomedical research have a far greater impact than merely the immediate cuts suffered by individual programs. These cuts have a lasting effect on the productivity of the nation's biomedical research effort that may take years to correct.

The federal objective of health improvement will not be fully realized by merely maintaining the *status quo*; federal funding for biomedical and behavioral sciences research should be increased. There are two reasons why more funding is needed. First, it costs more each year to maintain the same level of effort. In addition, as we penetrate more deeply to a true understanding of biologic processes, the research required to solve the next generation of scientific problems is increasingly more complex and expensive. An increase of 10 percent per year in annual appropriations for the NIH and ADAMHA is necessary to maintain the present scale of effort. Second, there needs to be real growth in federal biomedical research funding to take full advantage of currently available but unmet scientific opportunities. Such growth has been precluded in recent years by rising research costs. An additional 5 percent to 10 percent yearly increase in NIH and ADAMHA appropriations for the next 5 years would allow the system to expand to meet these challenges. Thus, the budgets for the NIH and ADAMHA should be increased by 15 percent to 20 percent annually for the next 5 years to restore the federal biomedical research effort to its traditional level of productivity and to more rapidly improve the nation's health.

III. PRIORITIES OF THE FEDERAL BIOMEDICAL AND BEHAVIORAL SCIENCES RESEARCH EFFORT

The present reexamination of federal research policy by the Congress and the administration must look beyond short-term, budget-driven decisions to the scientific, economic, and societal implications of these actions. Federal policy must recognize and preserve the unique strengths that have contributed to the system's overwhelming success. In addition to its focus on fundamental biological and clinical research, the system should continue to maintain diverse programs of research support that emphasize the vital role of investigator-initiated research. All research selected for funding should undergo rigorous technical review for scientific merit.

The system should continue to be predominantly extramural and academically-based to take advantage of the enormous national pool of creative scientific talent and resources, and to maintain the unique bond that exists between education and research. The intramural NIH and ADAMHA research programs should be maintained as a unique research resource. A diversity of institutions provides great flexibility to respond to scientific opportunities of varying degrees of scale and complexity.

An indispensable component of the federal biomedical research system is a strong program of research training. This should include the broad-based disciplinary and interdisciplinary training that is essential to produce scientists capable of working at the constantly changing frontiers of research. A key part of federal programs for research training is the institutional support provided to create an optimal training milieu. The heterogeneity of current federal research training programs should be maintained, with a continued emphasis on support for postdoctoral programs, which largely rely on federal funding.

The basic components of a sound federal program for the support of research training are in place. There are two areas of research manpower, however, that cause concern. First is the declining interest in careers in the biomedical sciences. Fewer young people are interested in and preparing for careers in biomedical research. The National Academy of Sciences (NAS) should undertake studies to identify reversible causes for this trend, and efforts should be made to address these causes.

There continues to be concern over the lack of well-qualified physician investigators. The declining ability of M.D. investigators to successfully compete for research grants has been attributed to inadequate preparation for research careers. Programs such as the NIH Medical Scientist Training Program and the Physician Scientist Awards seek to provide the highest quality training in basic science for physicians and should be models for the design of M.D. research training.

Often overlooked in the debate surrounding the scale of the federal investment in biomedical research are the research resources beyond the direct cost portion of the grant that are needed to sustain the fragile environment in which research is performed. For example, research equipment, which is becoming increasingly important as research becomes more complex, often is not recognized as an integral part of the ongoing program of federal biomedical research. State-of-the-art equipment should be provided to federally funded investigators. Maintenance of research facilities is another area in which increased federal investment is needed to maintain the research effort. Facilities needs in the biomedical sciences should be determined so that rational resource allocation can proceed. Programs for shared resources, such as the NIH General Clinical Research Centers and the Animal Resources Program, should be enhanced to increase the efficiency and productivity of the federal biomedical research investment. Flexible support funds for institutions, such as those available through the NIH Biomedical Research Support Grants, should also be increased. These funds are used to meet the unique and changing needs of individual institutions, enhance the research environment, and sustain their federal research programs.

Federal support for biomedical research also includes reimbursement to institutions for the costs associated with research that cannot be attributed directly to individual grants or contracts. Indirect costs policies are an area of disagreement among investigators, university administrators, and the federal government. All segments of the research community need to work toward agreement that those costs included in indirect reimbursement are true and necessary costs of research. At the same time, the government must make efforts to streamline and reduce the bureaucratic requirements that add unnecessary institutional administrative burdens and indirect costs. Methods must be found to provide a reasonable level of accountability in a cost efficient manner and to reduce excessive documentation.

IV. FORMULATION OF SCIENCE POLICY

There is concern about the quantity and quality of scientific advice available to Congress and the administration for the purposes of policy formulation. Efforts must be made to ensure that the Congress and the President receive impartial, realistic, and timely advice from the scientific community related to the goals of biomedical research and the means to achieve these goals. The advisory councils to the individual institutes at the NIH and ADAMHA should be more involved in the debate and make timely recommendations related to research policies and priorities to the Director of NIH and the Administrator of ADAMHA. Each agency should provide consensus advice to the Office of the Assistant Secretary for Health. The President's Office of Science and Technology Policy should include strong representation from the biomedical and behavioral science community so that the unique interests of the medical and life sciences are integrated into overall national science policy.

The NAS Institute of Medicine, which has served admirably in undertaking long term studies on key policy issues, should also undertake the task of providing immediate and impartial advice to the legislative and executive branches in such areas as budget and resource allocation in the federal program for biomedical and behavioral research. Such advice should represent a consensus of the scientific view responsive to public concerns.

I. THE GOAL OF THE FEDERAL EFFORT IN BIOMEDICAL AND BEHAVIORAL SCIENCES RESEARCH

The ultimate goal of the biomedical and behavioral sciences research conducted and supported by the federal government is to improve the health of the American people through the acquisition of scientific knowledge. This goal has a high priority for both the general public and the federal government. People today want and expect to have longer, healthier lives, free from the crippling disabilities caused by disease and aging. At the same time, the federal government has a basic responsibility, articulated in the Preamble of the Constitution, to promote the "general Welfare" of the people. One way is to work toward health improvement.

The federal role in health has evolved as the science of medicine has grown. Early efforts were devoted to sanitation, quarantine, and other hygienic measures. One of the earliest legislative initiatives was the passage of "an Act for the relief of sick and disabled seamen," which established the Marine Hospital Service—the predecessor of the Public Health Service (PHS)—in July 1798. As precise knowledge of the causes and treatments of human disease became the dominant influence in improving health, federal participation in acquiring this knowledge grew commensurately. Recognition of the role to be played by biomedical research in the battle against disease dates from the creation in 1879 of the National Board of Health, the first attempt at an organized, comprehensive, national medical research effort supported by the federal government. In 1887, the Laboratory of Hygiene, which served as the genesis for the National Institutes of Health (NIH), was founded.

The essential dependence of improvements in the nation's health upon fundamental biological and clinical research was reflected in the creation of the PHS. Since 1944, section 301 of the PHS Act [42 U.S Code 241] has stated that the agency:

> ... shall conduct and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the cooordination of, research, investigations, experiments, demonstrations, and studies related to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man. . . .

Clearly, the acquisition of new knowledge through biomedical research is only one component of the federal government's agenda to improve the health of its citizens. Better health for the American people can only be realized through determined efforts to expand the knowledge base through research and to apply this information through social and health care delivery programs. A broad-based approach, acknowledging the importance of an entire spectrum of federal responsibilities and initiatives, has enabled this nation to make great strides towards its identified health goals. The vast panoply of federal programs that contribute to the health of our citizens, ranging from toxic waste disposal to school lunches to Medicare, is administered by almost every federal agency and department. However, without the insight supplied by advances in fundamental scientific knowledge, federal efforts to improve health would be seriously limited. Research must continue to be protected and fostered as a critical component of the overall federal health policy.

Federally sponsored biomedical and behavioral sciences research is the foundation for the government's programs to improve the health of the American people.

Health research is conducted and supported by a number of federal departments and agencies. PHS agencies, including the Centers for Disease Control, the Food and Drug Administration, and the Health Resources and Services Administration, as well as the National Center for Health Statistics and the National Center for Health Services Research within the Office of the Assistant Secretary for Health, pursue various components of health research with a focus on clinical science, public education, health regulation, or health care delivery.

Agencies and departments outside the Department of Health and Human Services, such as Defense, Energy, and Agriculture, the Veterans Administration (VA), the National Aeronautics and Space Administration, and the National Science Foundation (NSF), also perform biological, biomedical, and health-related research. However, with the exception of the small VA and NSF programs, these departments and agencies focus primarily on targeted rather than basic research and emphasize the application rather than the development of novel scientific information. The NIH and the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) have as their primary mission the acquisition of fundamental knowledge through biologic and clinical research. Together they represent 75 percent of the federal investment in health research and development.

Over the past 40 years, advances in public health and health care have grown steadily more dependent on this expanding base of fundamental scientific knowledge, which provides the scientific opportunities that ultimately and often unpredictably lead to the solution of specific health problems. The unique focus of the NIH and ADAMHA in supporting and conducting fundamental biomedical and behavioral sciences research has fostered the development of the world's greatest scientific enterprise. This emphasis must continue.

Increasing pressures to extend the missions of the NIH and ADAMHA to include health care delivery, public education, regulation, and other goals of national health policy must be resisted, and these non-research objectives undertaken by other components of the PHS, by industry, or by medical educators and practitioners as appropriate. Along a continuum from basic discoveries to the full application of such discoveries to patient care, the efforts of the NIH and ADAMHA should continue to be devoted to the acquisition of new knowledge and to the clinical research necessary to translate this knowledge into effective therapies. Demonstration projects, educational programs directed at professionals and the public, and patient care represent valuable and necessary efforts to achieve the national goal of improved health, but they should not compete for the limited financial and personnel resources available to sustain and expand the knowledge base.

The research mission of the NIH and ADAMHA must be preserved. Non-research components of the federal health agenda such as public education and health care delivery should be entrusted to other federal agencies or, when appropriate, to the private sector.

On another front, the limited federal resources available for biomedical research are being threatened by the very success of the system these resources have created. Recent research advances, such as those in molecular genetics that spawned an entire biotechnology industry and contributed to national prestige and economic development, have generated pressures to divert federal research resources to achieve non-scientific goals. Examples of such broader societal concerns include using scientific investment as a mechanism for regional economic development, maintaining the competitiveness of American industry in the world marketplace, promoting geographic diversity of research centers, and enhancing the participation of all segments of the population in a society based on science and technology.

However laudable such goals may be, a reordering of research priorities specifically for the purpose of accomplishing these non-scientific objectives will only serve to divert scarce resources from the primary mission of acquiring knowledge to improve health. Furthermore, on the basis of 40 years of past experience, one can reasonably expect that many of these societal benefits — including economic development, world prestige, and equity of access to new therapies and to careers in science — will continue to be achieved as a consequence of the fulfillment of the primary goal of federal biomedical research. In fact, because most of these other societal goals can be achieved only as a result of success in generating a base of fundamental knowledge, a diversion of resources away from such research would eventually undermine the success of the entire federal biomedical and behavioral sciences research effort, and thereby be self-defeating.

The reordering of research priorities to achieve non-scientific objectives diverts limited resources from the principal goal of acquiring new knowledge to improve health and serves to weaken the overall federal biomedical research effort.

II. THE SCALE AND SCOPE OF THE FEDERAL INVESTMENT IN BIOMEDICAL AND BIOBEHAVIORAL RESEARCH

The long-standing federal commitment to investment in biomedical and behavioral sciences research as a way to improve the health of the American people has been tremendously successful in terms of scientific achievement and societal gain. This support has led to the discovery of biological and clinical knowledge that has extended the length and improved the quality of life for millions of people, thus benefiting the nation by increasing the well-being and productivity of its citizens. In addition, these advances have provided substantial gain for the national economy. It is estimated that the rate of return on every $1 invested in biomedical research is $13. For example, the introduction of lithium treatment for manic-depressive disorders has saved an estimated $6.5 billion, far exceeding the total federal investment in the National Institute of Mental Health since its inception.

The federal contribution to biomedical research remains a unique one because of the continued emphasis on basic biological and clinical investigations. Much of this research would be unfunded and therefore would not be done if not for federal resources. The system of biomedical research that has evolved with the benefit of federal support is so extensive that it must rely primarily on continued federal investment to sustain the present effort.

Historically, the federal government has followed a pattern of continued growth in the annual budget for biomedical research. In the early years these increases provided exceptional real growth, whereas more recently, large annual increases have been necessary just to achieve stable purchasing power (Figure 1). Each year it costs more for the system to support the same level of research, i.e., the same number of research projects, because of increases in equipment and personnel costs. The Biomedical Research and Development Price Index (BRDPI) provides some measure of the cost growth characteristics for research in the medical sciences. This index has increased by an average of 7.4 percent per year between 1975 and 1984 (Table 1).

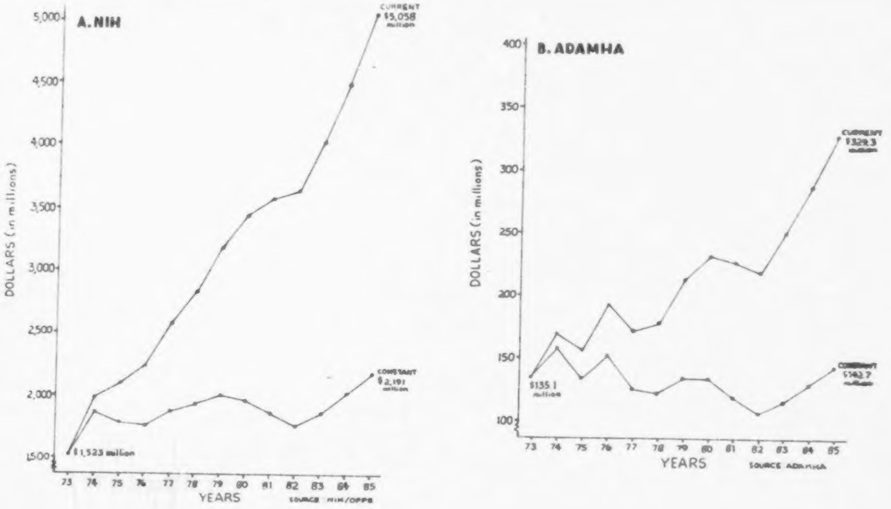

Figure 1. Research and research training in current and constant dollars, fiscal years 1973-1985. 1A. NIH funding; 1B. ADAMHA funding.

In addition, the information provided by current research often leads to more advanced and complex scientific inquiries. This next generation of research is more costly because of the need for more complex equipment and more highly trained, specialized technicians. The BRDPI probably underestimates the increased costs related to the increasing complexity of research. For example, the direct cost of individual research project grants increased an average of 8.2 percent between 1975 and 1984 (Table 2). This was in spite of mandated reductions of between 2 percent and 6 percent in direct costs in several of those years. These direct costs also did not provide needed equipment in many cases. As a result, the increasing direct cost of project grants only partially reflects the actual cost associated with increasingly complex research.

Increased funding for biomedical research is necessary to sustain the current effort because of the increasing complexity and cost of biomedical research. An increase of 10 percent per year in the annual appropriations for the NIH and ADAMHA is necessary to meet this need.

The situation with respect to funding for research and research training at ADAMHA is complicated by the fact that the agency experienced a one-third reduction in constant dollar purchasing power between 1974 and 1982. In spite of the significant funding increases that have been provided between 1982 and 1986, the ADAMHA funding base has not been completely restored to the 1974 level (Figure 1b). In 1985, this shortfall amounted to approximately 12 percent of the total ADAMHA budget for research and research training.

Funding for ADAMHA research and research training needs an additional one time *increase of approximately 12 percent to compensate for the reduction in purchasing power that occurred between 1974 and 1982.*

We must not only sustain the present effort; the national commitment to steadily improving the health of the American people demands real growth in the federal program for biomedical and behavioral sciences research. Why is continued growth in the biomedical research effort essential? And how much federal investment is necessary to ensure this growth? The answer to both questions is scientific opportunity. The federal biomedical research effort must grow to avail itself fully of the explosion of opportunities currently available in the biological sciences. There are indications that this may be the beginning of a "Golden Age" of discovery in biological and medical research. Former White House Science Advisor George A. Keyworth, testifying before the House Committee on Science and Technology in February 1985, said that the "biological sciences stand on the brink of understanding that I can only liken to the brink that Einstein saw for physics in 1905." A wise federal investment policy would be to ensure that the combination of federal and private resources devoted to fundamental research in the medical sciences is sufficient to take full advantage of the opportunities for significant discovery. Only this way can the research system be tuned to maximal productivity and fully reap the already significant federal investment in advancing knowledge.

Increased federal support for biomedical research is essential to take advantage of currently unmet scientific opportunities.

Table 1. BIOMEDICAL R&D PRICE INDEX

Year	BRDPI Index	Percent Increase
1975	100.0	—
1976	107.5	7.5
1977	116.0	7.9
1978	124.7	7.5
1979	134.9	8.2
1980	147.2	9.1
1981	162.3	10.3
1982	174.2	7.3
1983	182.8	4.9
1984	189.3	3.6

Source: NIH Data Book 1985

Table 2. AVERAGE DIRECT COST OF NIH TRADITIONAL RESEARCH PROJECTS (RO1) (current dollars in thousands)

Year	Average Direct Cost	Increase
1975	$41.0	—
1976	43.7	6.6
1977	48.3	10.5
1978	52.3	8.3
1979	55.3	5.8
1980	59.0	6.7
1981	64.2	8.8
1982	69.1	7.6
1983	74.7	8.1
1984	83.3	11.5

Source: NIH, DRG, Statistics and Analysis Branch

Scientific opportunities far exceed the current federal investment. A rational approach to the question of the scale of growth — and the increase in federal funds necessary to achieve this growth — would be to base the federal investment on present or anticipated scientific opportunities. This might be accomplished in several ways. One would be to link the amount of funding to the availability of high quality scientific ideas, as measured by research proposals receiving excellent scores at scientific merit review. Technical merit is rated on a scale of 100 to 500, with 100 being the best. Since 1972, there has been a steady growth, averaging more than 10 percent per year, in the number of high quality (scores of 200 or less) research project applications (Figure 2).

High quality proposals not supported because of insufficient resources represent the capacity of the federal biomedical research enterprise to grow without compromising the quality of the science being funded. The increasing numbers of high quality research ideas that have gone unfunded in the last few years demonstrate both the existence of additional scientific opportunities and the need for continued growth to take full advantage of them. For example, there were approximately 1,100 NIH competing research project applications with very high technical merit ratings that were not funded in fiscal 1983. In fiscal 1984, this number rose to 1,500.

> *High quality merit-reviewed research project applications that cannot be funded are one measure of immediately available scientific opportunity.*

Unfunded applications are one way to gauge unmet opportunity and determine the appropriate scale of the federal investment. Scientific opportunity also can be assessed by a process of periodic formal review. Such review might be conducted every five years by a panel of distinguished researchers drawn from different biomedical and behavioral science disciplines under the auspices of the National Academy of Sciences (NAS). This panel would review the progress being made in various research areas and attempt to identify fields of research that are expanding and would benefit from additional funding. This overview perspective also has the advantage of providing a basis for longer-range fiscal planning. For example, the panel might identify a particular area of research that has produced a significant number of first-rate research ideas and is clearly ripe for an increased investment. Another field of research might be seen as having great promise but few researchers, thus requiring a gradual increase in funding to sustain the field as it attracts more investigators. Recent examples of such blue-ribbon panel reports prepared under NAS guidance include the Pimentel report on *Opportunities in Chemistry*, the Institute of Medicine report on *Research on Mental Illness and Addictive Disorders: Progress and Prospects*, and the current National Research Council Committee to identify Research Opportunities in Biology.

> *A panel of distinguished scientists, under the auspices of the National Academy of Sciences, should provide a periodic formal review of the fields of biomedical and behavioral research to identify scientific opportunity and the desirable level of investment.*

The last 40 years have shown the wisdom of providing for continued growth in the federal biomedical research budget. Such growth has been essential to meet past scientific challenges and has provided the basis for the multiplicity of medical advances that have enriched human life. This growth also has proven to be a prudent investment in the future because it has afforded biomedical researchers new challenges and new opportunities. But this growth cannot be obtained merely by shifting funds from one budget mechanism to another. To take advantage of expanding scientific opportunities and to reach the full potential of this immensely productive national research program, an additional 5 percent to 10 percent yearly increase in NIH

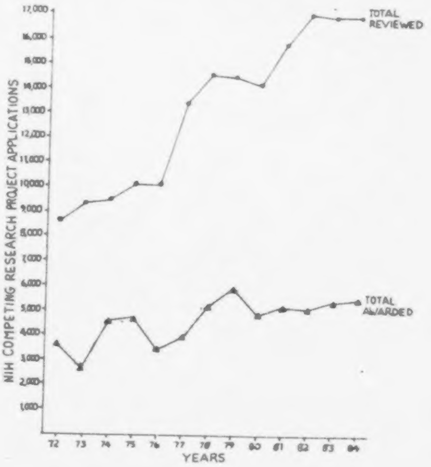

Figure 2. NIH competing research project grant applications; total applications reviewed and total grants awarded, fiscal years 1972-1984. Applications given priority scores of 200 to 250 in merit review are shown as a gray zone.

and ADAMHA appropriations for the next 5 years would be a wise and cost effective federal investment. This increase would be in addition to the 10 percent needed to sustain the current level of effort.

> A total *annual increase in appropriations for biomedical and behavioral research of from 15 percent to 20 percent for the next 5 years is needed both to sustain the present research effort and to take advantage of new opportunities.*

The present political and fiscal pressures occasioned by the growing federal budget deficit are challenging this long-standing federal commitment to the biomedical research effort. Despite these pressures, any reevaluation of policy must acknowledge that reductions in research funding in attempts to reduce the deficit in the short-term will have serious repercussions for biomedical research — and thus the health and welfare of the American people — in the long term. Biomedical research is a long term endeavor; the nation's medical schools and academic medical centers took years to develop the talent and resources necessary to achieve the current level of productivity. Reductions in federal support for biomedical research have a far greater impact than merely the immediate cuts suffered by individual programs. These cuts have a lasting effect on the productivity of the nation's biomedical research efforts that may take years to correct.

The current fiscal climate requires a careful husbanding of federal resources, but the potential of the federal biomedical research enterprise and the opportunities that are available argue that such husbanding includes *enhancing* the federal investment in biomedical research. Those who wish to reduce federal spending for health care research and at the same time cut the costs for providing the basic safety net of social service and medical care programs must realize that it is this very research that offers a significant prospect for eventually reducing expenditures for health care. An era of deficit reduction and decreasing federal budgets is, paradoxically, not the time to cut federal investment in research. Investment in basic research not only fuels the economy with jobs and funds, it also produces discoveries that improve the lives of our citizens and ensures our preeminence in world markets as well as domestic prosperity.

III. PRIORITIES OF THE FEDERAL BIOMEDICAL AND BEHAVIORAL SCIENCES RESEARCH EFFORT

The organizational structure for the conduct of biomedical and behavioral sciences research that has evolved as a result of the ongoing investment of federal funds has been highly successful in achieving its scientific goals of improving the quality of life for the American people. These triumphs were possible, in large part, because of several unique strengths of this system. It is imperative that federal policy recognize these strengths and preserve them in the face of increasingly stringent economic constraints by giving them the highest priority for the limited federal resources. These characteristics are:

1) emphasis on fundamental biological and clinical research;

2) emphasis on investigator-initiated research, selected through rigorous review for scientific merit;

3) support for predominantly extramural, academically-based research;

4) support for the research training system necessary to continue the flow of creative investigators; and

5) provision of the diverse resources necessary to sustain the extramural, investigator-centered research enterprise.

FUNDAMENTAL RESEARCH

The federal investment in biomedical research traditionally has placed a greater emphasis on basic or fundamental research than on targeted or applied research. Federal policy makers have acknowledged that the discovery of new scientific knowledge through basic biological research is the cornerstone in our understanding of human disease and its eventual prevention or treatment.

Such research includes as a key component clinical investigation to advance our knowledge of human biology and pathology. Clinical research is not only the crucial link where basic biological knowledge is both developed and utilized; it also serves to identify areas where further basic research is necessary.

In a time of fiscal constraint, this emphasis on fundamental research should be continued and strengthened. Federal funds should support heavily this portion of the spectrum of biomedical research, because other sources of support for it are not available. In some areas of applied research, such as large scale clinical trials where the general efficacy of already developed therapies is being tested, efforts should be made to identify other resources, such as patient care or pharmaceutical industry funds, to share in the support of such research.

In general, the federal biomedical research effort should not extend into areas of applied or targeted research where the goal is the commercial development and production of diagnostics and therapeutics. The biomedical industry has both the resources and the expertise to carry out technology transfer for commercial development in a much faster and more efficient manner than the federal government could hope to accomplish; indeed, survival in today's competitive marketplace demands the ability to translate basic scientific discoveries into practical applications. A prime example of this is the growth of the bioengineering industry out of basic discoveries in molecular genetics.

> *The federal investment in biomedical research should continue to emphasize fundamental biological and clinical research. Such research is the source of the new knowledge needed to accomplish advances in health care.*

INVESTIGATOR-INITIATED RESEARCH

Investigator-initiated research is the vital core of the federal biomedical research effort. Investigator-initiated grants have proven most productive for exploring and developing new scientific opportunities. This approach utilizes the unique talents of thousands of individual scientists to sustain a broad-based, flexible program of biomedical research. Investigators pursue their own ideas and use their scientific instincts and laboratory experience to develop new approaches to research problems and to follow up on unexpected findings. Investigator-initiated research may occur in multi-investigator and multi-disciplinary settings; its hallmark is that scientists formulate the proposed research whether through a program project, center, or other funding mechanism. The past has shown the value of a wide range of funding mechanisms to support biomedical research. The trend has been toward large numbers of relatively small projects, which provides NIH and ADAMHA with the flexibility to shift the emphasis in programs as scientists shift their research without disrupting large bureaucratic enterprises.

In a time of limited resources, however, the value of this far-ranging, broad-based fundamental research may not be immediately obvious to the public, which is understandably more concerned with short term applications of scientific knowledge to specific diseases. Yet it is in such times of fiscal constraint that we should assign the highest funding priority to this most essential and creative component of the biomedical research effort.

The highest funding priority should be given to investigator-initiated research projects because these provide maximum creativity and flexibility in the research system.

EXTRAMURAL RESEARCH

The founding genius of our federal biomedical research effort was the decision to seek new knowledge in the biosciences predominantly through a system of awards to individuals in institutions all across the nation. This decision to fund the best and most promising scientific ideas regardless of where they originated sparked the development of the outstanding biomedical research enterprise the nation now enjoys. The research agencies have been able to tap the human, organizational, and physical resources of the entire country to create a truly national effort.

This extramural approach provides several distinct advantages. First, a vast national pool of creative scientific talent can be drawn from and the resources of many diverse institutions can be joined with those of the NIH and ADAMHA to further the federal biomedical research effort. This large and heterogeneous assortment of institutions has the capacity to undertake research projects of varying degrees of scale and complexity. Such a system encourages maximum creativity and flexibility from individual investigators or teams of researchers in responding to scientific opportunity.

Another advantage is that this research is conducted primarily in academic settings. In fiscal 1984, 75 percent of NIH extramural awards went to institutions of higher education, and 52 percent went to medical schools and their affiliated hospitals. The coupling of the research and educational efforts is a unique strength of the American university system. In most graduate programs, students are trained while they participate in research, thus yielding a dual dividend: talent and knowledge. The search for new knowledge and the dissemination of established learning make invaluable contributions to one another.

The diversity of institutions that participate in the extramural system also enables and encourages a cross-section of this nation's people to participate in the federal biomedical research effort, thereby benefiting both the institutions themselves and society as a whole.

The federal biomedical research enterprise should remain predominantly extramural and academically based.

INTRAMURAL RESEARCH

This emphasis on extramural research should not detract from the importance of the remarkably vigorous and productive intramural programs at the NIH and ADAMHA. The wealth of basic biological and clinical knowledge developed in these programs has contributed significantly to our current understanding of human disease. The recent achievements in research on the viral agent for acquired immune deficiency syndrome (AIDS) once again demonstrate the strength of the intellectual and creative resources of the intramural program. The Clinical Center at the NIH is the site of innovative clinical investigations into the mechanisms underlying human disease and should continue as a vital component of the intramural program. The presence of this active research effort at NIH also enhances the quality and sophistication of the administration of the extramural program.

In addition to the research itself, the NIH and ADAMHA programs make significant contributions to research training and serve as an important personnel resource for the extramural research community. A free flow of ideas and personnel between the intramural and extramural programs strengthens both and should be encouraged. The ability of the intramural program to recruit and retain well-qualified senior scientists and administrators should be enhanced. Such initiatives would ensure the continuation of the competent leadership provided by the senior staff at the NIH and ADAMHA, which is critical to the success of not only the intramural programs but also the entire extramural research effort.

The intramural research program at NIH and ADAMHA should be continued. Programs for research trainees and investigators to participate in intramural research should be strengthened and expanded. Initiatives should be undertaken to attract and retain exceptional senior scientists and administrators at the NIH and ADAMHA.

SCIENTIFIC MERIT REVIEW

The concept that the significance or merit of a scientific proposal is judged best by other scientists is not new; it has existed in various forms since the 17th century. Even so, the post World War II decision to allow scientists a primary role in determining the merit basis for the allocation of federal funds for scientific research was a rather bold one that did not command universal assent. The record of the past 40 years, however, has shown the wisdom and value of scientific merit review.

Recently the equity of the merit review system has been challenged both from outside and within the science community. As science and the federal investment in it have grown in scale and impact, the desire to participate in and partake of this success has increased commensurately. The public, and their elected representatives, are increasingly interested in focusing these enormous talents and technical resources on the diseases that to them are most urgent. Judgment of the merit of research proposals on the criteria of scientific excellence and opportunity is increasingly at odds with congressional concern for equal distribution of scientific resources.

Many scientists also have joined the critics of the merit review system. These criticisms are probably more a consequence of the inordinate pressures brought to bear on the scientific review system because funds are not sufficient to keep pace with the burgeoning scientific opportunity in biomedical research. Scientists with good ideas that are not funded increasingly challenge the ability of the merit review system to make fine distinctions between the quality of ideas.

The concept of peer review is sound. The primary basis for allocation of federal funds for biomedical and behavioral sciences research must be the scientific quality of the research proposals submitted. Scientific quality is best judged by scientists who are familiar with the field of research in question and can, therefore, address issues such as scientific opportunity and technical merit. The record of the peer review system over the last 40 years speaks for itself. Through peer review for scientific merit and advisory council review for program priority, federal funds awarded to a remarkable array of institutions and scientists have led to world preeminence for American biomedical research and significant improvements in human health.

> *The allocation of federal funds for biomedical and behavioral research should continue to be based on the system of scientific merit review of proposals. This system is best able to identify scientific excellence and to insure the quality of the federal investment. Priorities for funding and long range planning to meet national goals should be determined by the institute advisory councils and funding decisions within these priority areas should be based on scientific merit.*

Despite all of the concerns expressed by scientists and lay observers about the potential for abuse and conflict of interest inherent in any system that employs peer judgments, the peer review systems that have evolved at the NIH and ADAMHA remain the best and most objective method available to evaluate scientific merit. The scale of the review system, with over 1,000 scientists participating and one-quarter of the membership changing every year, does much to ensure that the majority of the research community, rather than a select few, eventually serve as evaluator as well as applicant. The system works; it must be preserved and strengthened. There must be continued attention to maintaining a balanced representation on review groups and to insuring the quality of the peer review process in order to provide the best scientific review.

> *There should be a periodic, formal examination of the mechanisms for merit review of grant applications used by NIH and ADAMHA. Such review will insure that equitable peer review procedures are used to identify the best science.*

RESEARCH TRAINING

This nation's remarkable achievements in biomedical research would not have been possible without strong federal support for the training of research manpower. A reservoir of highly trained biomedical scientists is indispensable to the national biomedical research system and must be replenished continually if we are to maintain our current research capabilities and take advantage of future opportunities. To ensure the continued availability of sufficient skilled scientists to meet these national research objectives, significant federal involvement in research training must continue.

The Current System

Federal biomedical and behavioral research training programs must provide a variety of training mechanisms and encourage the broad-based disciplinary and interdisciplinary training essential to produce scientists capable of productive careers within a profession with constantly evolving frontiers. This support ranges from formal research training programs funded under the authority of the National Research Service Awards (NRSA) to support of trainees as research assistants on individual project awards.

In research intensive universities, as many as 30 percent of Ph.D. candidates are supported as research assistants on federal research grants; nationally, almost half of all Ph.D. postdoctorals and 5 percent to 10 percent of M.D. postdoctorals are supported through research project funds. While these funds do not support the training environment per se, they are an appropriate source of support for trainees during those portions of training when they can and should function as integral members of individual research teams.

Currently, federal training programs provide approximately 15 percent of Ph.D. predoctoral support, but 34 percent of Ph.D. postdoctoral and 45 percent of M.D. postdoctoral research training support in the biomedical sciences. This federal emphasis on support for graduate, and even more for postgraduate, programs must continue. It is at the postgraduate level that those talented individuals who will make future creative contributions to biomedical research are identified, and at this level that non-federal sources of support for such advanced training diminish, leaving a natural and essential role for federal programs.

A further important component of federal support for advanced trainees is the program of research career development awards through the NIH and ADAMHA. This varied portfolio of awards, designed to support the transition from research trainee to fully independent, funded investigator, is uniquely tailored to the needs of differing career stages and to addressing shortage areas such as physician investigators.

The heterogeneity of federal support mechanisms for biomedical and behavioral research training must be maintained. The mixture of support from different agencies and under the aegis of different programs, ranging from those specific for training to components of research or clinical programs, should be continued. Federal programs should continue to emphasize support of postdoctoral programs.

NRSA training programs include both institutional training grants and individual fellowship awards. At the recommendation of the National Academy of Sciences Committee on National Needs for Biomedical and Behavioral Research Personnel, 85 percent of NRSA grants are made to institutions. While the individual awards based upon competitively reviewed research proposals are an important mechanism for supporting advanced research fellows, the majority of funds should continue to be provided in the form of institutional training grants. Such grants enable institutions to amass sufficient trainees and the critical institutional resources to provide a proper and broad-based training milieu.

Federal programs should continue to emphasize and strongly support the institutional components of research training as well as trainee stipends to provide an optimal training milieu.

The exponential expansion of the "new biology" necessitates an average investment of ten years of training beyond the baccalaureate degree. The length of this training requires large scale programs involving extensive and long term commitments of personnel and laboratory resources in order to sustain sufficient numbers of trainees at each stage to eventually yield a small cadre of research scientists. The NAS estimates that nationally there are at any one time some 60,000 Ph.D. predoctoral candidates and 15,000 Ph.D. and M.D. postdoctorals in training in the biomedical and behavioral sciences. It is estimated that each year approximately 2,200 Ph.D.s, 1,200 M.D.s, and 150 M.D./Ph.D.s complete the entire training sequence and emerge from postdoctoral fellowship programs fully trained for careers as independent investigators.

These estimates emerge from the extensive manpower study conducted biennially by the NAS Personnel Needs Committee. This committee was chartered by the National Research Act of 1974 to develop projections of manpower needs and make recommendations regarding the appropriate scale and scope of federal training programs in the biomedical sciences. The data collected by this committee have proven useful in evaluating the current status of research manpower in the clinical, basic biomedical, and behavioral sciences as well as allied health sciences and nursing research.

The federal government, through the National Academy of Sciences, should continue to monitor all aspects of research training in the biomedical and behavioral sciences.

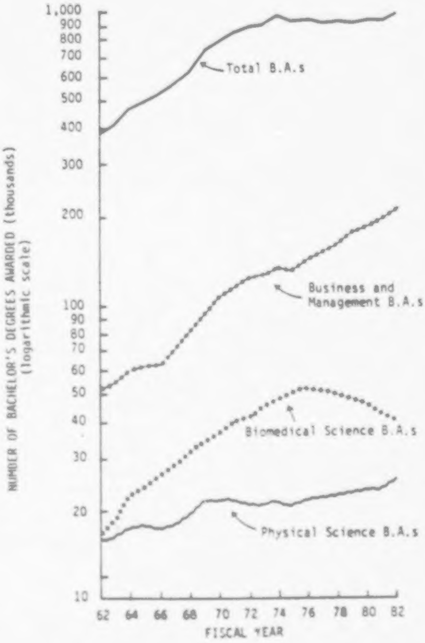

Figure 3. Bachelor degrees awarded in biomedical science fields compared to other fields, fiscal years 1962-1982. (Source: NAS Personnel Needs Committee, 1985 Report)

Unfortunately, while the present effort can be quantitated, projections of future manpower needs in rapidly evolving disciplines, based on unknown future scientific opportunity, cannot be made with a high degree of accuracy. The unpredictability of the rate of advance in various scientific fields and the long lag time between identification of the need for additional manpower and the production of more fully trained investigators argue for a system that makes only the most general estimates and tends to err on the side of overproduction. Elaborate efforts to quantify the unquantifiable should yield to ensuring an excess of broadly trained personnel in a system with sufficient flexibility, adaptability, and re-training capacity to provide a continual supply of new young researchers with the capability to pursue these dimly forseen opportunities.

Future Concerns

The basic components of a sound federal program in support of research training in the biomedical sciences are in place. Continued attention to the appropriate scale of these programs to meet anticipated manpower needs and to the provision of adequate trainee support and institutional resources within each program are essential. In two areas, however, there is concern that research manpower needs are in jeopardy.

First, there is growing apprehension related to the declining interest in careers in the life sciences. The number of potential applicants for Ph.D. programs in biomedical research has declined over the past decade, and current indications are that this trend will continue. The number of people graduating with baccalaureate degrees in the life sciences has been decreasing since 1976 (Figure 3). Current estimates by the NAS are that the number of first year graduate enrollments in the biomedical sciences peaked in 1978, and has been declining ever since. The growing number of foreign nationals in Ph.D. programs should be assessed for its impact on future American scientific productivity. Medical school applications have fallen by 23 percent since 1974. In addition, training program directors in the biomedical sciences have noted deterioration in the quality of the predoctoral applicant pool, increased numbers of foreign nationals in these training programs, and an increased competition for qualified postdoctoral trainees. The trends are becoming apparent: fewer young people today are preparing for careers in the biomedical sciences.

These trends must be monitored closely, and studies undertaken to identify reversible causes for these declining enrollments. Anecdotal evidence suggests that careers in biomedical research appear less attractive to young people than they once did. The fierce competition to sustain grant support, increasing administrative and bureaucratic burdens, reduced freedom and flexibility to pursue independent research ideas, and prolonged training are all cited. Efforts to document these or other causes and to reverse these trends should be undertaken. Specific federal programs to recruit and enhance the pool of qualified predoctoral candidates should be funded.

> *The NAS should closely monitor worrisome trends toward diminishing interest in life science careers. Studies should be undertaken to identify reversible causes for this decline in the student groups from which future biomedical scientists are recruited.*

Equally troubling is the continued lack of sufficient well-qualified physician investigators, first identifed in the late 1970s. The percentage of physicians serving as principal investigators on NIH investigator-initiated research project grants (RO1 awards) continues to decline (Figure 4) and the number of M.D. postdoctorals in the NRSA program remains below recommended levels (Figure 5). Clinical investigators make two vital and indispensable contributions to biomedical

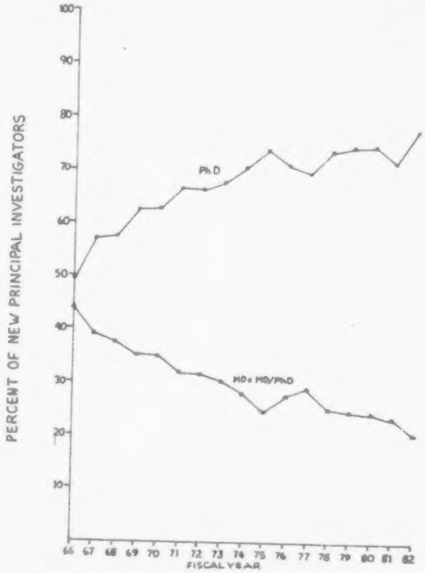

Figure 4. New NIH research project awards charted by type of earned degree of the principal investigator, fiscal years 1966-1982. (Source: NIH)

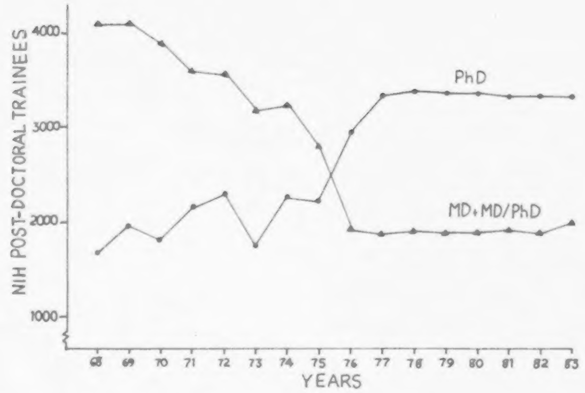

Figure 5. Postdoctoral traineeships and fellowships awarded by NIH to candidates with M.D. and M.D./Ph.D degrees as compared with those with the Ph.D. degree only (full-time equivalent trainees and fellow), fiscal years 1968-1983. (Source: NIH)

research. First, there are certain types of research that are best done or can only be done by individuals with clinical training. Second, M.D. investigators uniquely employ their clinical knowledge and experience to identify important problems and needs for basic research. Physician investigators truly serve as vital bridges to achieve the necessary synthesis of new basic knowledge with its application to clinical situations and problems.

While the number of M.D. and M.D./Ph.D. applicants for research funding have remained relatively steady during the last 10 years, the percentage of grant applicants and recipients with clinical degrees has declined. This is because of the increasing numbers of Ph.D. applicants and the growth in the total number of grants funded. After a thorough examination of threats to this "endangered species," the NIH concluded that the declining ability of M.D. investigators to compete successfully for research grants and to successfully sustain full research careers can in large part be attributed to inadequate preparation to deal with the increasingly complex research required to make the next generation of advances in biological research. NIH has shown that the duration of research training correlates with later success in obtaining competitive research funding (Figure 6).

To remedy this problem, NIH has focused efforts since 1980 on developing programs to provide better research training opportunities for M.D.s. NIH has strongly recommended that M.D. trainees on institutional research training grants spend a *minimum* of 2 years and preferably longer in an advanced program of research training. There have also been attempts, thus far unsuccessful, to increase the number of M.D.s on both institutional and individual training grants in the NRSA postdoctoral program. The distribution of career development awards has shifted to ensure that 50 percent of awardees will be young physician scientists. A special career development program — the Physician Scientist Award — was created to provide M.D.s with 5 years of training in both basic and clinical research. Renewed emphasis has been placed on generating interest in research careers among medical students by a short term research program and a joint venture with the Howard Hughes Medical Institute to support year-long research experiences for medical students at the NIH. Resources for the highly successful Medical Scientist Training Program (MSTP) have continued to increase. The MSTP program is an M.D.-Ph.D. program that provides participants with a firm grounding in basic biomedical research while supporting their training as physicians. Unfortunately, increased resources for this program have only kept pace with rising costs, and there has been no increase in the number of trainees or training sites since 1978.

There are many more qualified applicants and training sites than can be accommodated in the research intensive MSTP and Physician Scientist Award programs, and efforts should be made to increase the number of trainees in these programs as well as the number of M.D. trainees in rigorous institutional training grant programs. All of these initiatives are laudable and target identified causes for decreased physician participation in research. Physician investigators must have

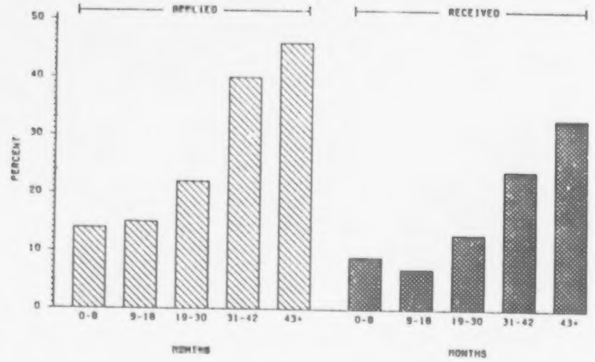

Figure 6. Percentage of M.D. postdoctoral trainees who applied for or received a research grant, by length of supported training, first year of training 1976-1980. (Source: NIH/OPPE/DPA)

basic and thorough research training comparable to that received by Ph.D.s. Such training is not an integral part of medical school or clinical residency programs and must be fully provided within the research portion of M.D. investigator training.

Recent federal emphasis on programs to train physician scientists should be continued and expanded to counter their declining participation in research. Efforts should focus on increasing the quality and duration of scientific training for M.D.s.

RESEARCH SUPPORT

Federal support for fundamental, investigator-initiated, extramural research necessarily involves more than just the direct cost portion of the grant. It includes all of the resources needed to ensure that the individual investigator or group of scientists can actually do the research. This is particularly true in fiscally austere times, when one possible policy option is to withhold certain elements of research support to sustain an arbitrarily determined number of grants with partial support. It should be a major goal of federal policy during periods of fiscal constraint to ensure that the scale of the effort does not exceed that which can be appropriately supported.

The number of extramural grants awarded each year should be maintained at the highest level at which adequate funds for full direct grant costs and research support resources can be provided.

Another factor to be considered is that even though the core of the federal biomedical research enterprise consists of ideas generated by individual investigators, the research support necessary for the realization of these ideas often extends far beyond that awarded to the individual scientists themselves. The federal investment in biomedical research must not only support the individual projects but also the entire system or environment in which the research takes place.

To the extent that these resources are beyond the scope of the direct costs on individual research awards, they must be available to ensure that maximal research productivity can be sustained. As funding for biomedical research has plateaued, these resources have become increasingly constrained. This frugal approach is perhaps understandable as a short-term strategy for coping with limited resources, but now it is becoming a *de facto* long term policy that is increasingly counterproductive as resources accumulated during years of expanding biomedical research investment become depleted in rapidly advancing fields.

Research support is particularly critical at a time when the academic medical center is threatened by resource constraints on all fronts. Pressures to reduce health care costs are reducing the institutional support derived from the education and clinical practice efforts of the faculty; medical school applications and enrollments are declining in response to a perceived physician surplus; and access to capital in the nonprofit sector to restore or replace aging equipment and facilities is increasingly limited.

While responsible policy in the present era would support a cautious approach to investment in research resources and seek in all instances to maximize the research return on these investments, this area of federal investment policy deserves concerted study. When "making do" hobbles research productivity, it is unsound public policy. It should be the responsibility of the federal government to monitor the resources of the extramural research community with a view to understanding what is needed to maintain the national research capacity.

> *The NIH and ADAMHA should analyze the research capability and anticipated needs for major equipment and facilities to maintain the biomedical and behavioral research capacity of the extramural community.*

Direct Costs

During the past several years, the direct cost portion of biomedical research grants has risen dramatically. Much of this increase can be attributed to the increasing complexity of research in the biological sciences. This advance in science is reflected in proportional increases in all components of direct costs. However, personnel costs continue to account for over two-thirds of the direct cost of research grants. Salaries have increased because of the need to hire technicians with more advanced training to cope with advancing technology. Salaries for research personnel have also increased because of the need to make them more competitive with industry and other occupations to attract and keep well-trained personnel in academic laboratories. Efforts to limit or reduce direct costs below study section recommendations would have a chilling effect on biomedical research by making it difficult to hire and retain sufficient skilled laboratory personnel.

> *Direct costs for biomedical and behavioral sciences research grants should be provided at amounts determined to be adequate by scientific review.*

Equipment

Equipment is a crucial component of a successful biomedical research effort; it has become increasingly vital over recent decades as research has become more complex. Between 1983 and 1985, the NIH examined the state of research instrumentation in the extramural research institutions through a study of the status of equipment, present expenditures, and projected needs. In the field of biomedical research the greatest need continues to be for equipment of a scale that can be provided through direct grant programs. The recent NIH/WESTAT study pinpointed a major need for equipment in the $10,000 to $50,000 range. To achieve optimal research productivity and remain at the forefront of science, appropriate equipment needs should be met as an integral part of the ongoing federal biomedical research progam.

> *Federal policies should encourage the provision of state-of-the-art equipment for biomedical research through direct award on individual grants or Shared Instrument Grant awards.*

A recent interagency study[†] was also completed that explored ways of improving the purchase and management of research equipment to reduce waste and improve utilization. Federal policy in many areas impinges on the ability to obtain university research equipment. Tax policy can be constructed to encourage corporate donation of equipment; federal depreciation schedules can be accelerated in recognition of the rapid obsolescence of research equipment; novel arrangements can be tried to facilitate direct grant purchase of more expensive equipment by spreading the purchase cost over several years of the grant or among several grantees; and indirect costs policies can be reviewed with an eye toward encouraging economies of use and purchase for state-of-the-art equipment.

> *Federal policies that impinge on acquisition, maintenance, and use of research equipment should be reviewed to streamline procedures and encourage economies of use and purchase. State-of-the-art equipment must be appropriately available for use in federally funded research projects.*

Shared Resources

As increasingly diverse scientific opportunities compete for limited resources, sound federal research policy must turn to ways in which needed resources can be used most efficiently and productively. One approach is through programs that provide research resources for shared use by entire institutions or even the entire research community. NIH provides such support programs through its Division of Research Resources. The General Clinical Research Centers (GCRC) Program supports 75 clinical research centers at our nation's academic medical centers. By providing centralized facilities and core laboratory and clinical personnel, these centers support the clinical research being performed on over 3500 project grants. These unique facilities with personnel trained in research procedures have been a remarkably efficient and productive resource, and full support of a vigorous GCRC grant program is warranted. The Animal Resources Program also provides critical resources for research by supporting regional primate centers, laboratory animal sciences program grants, and a program to provide institutional animal resource improvements. In view of the well documented need for substantial investment to upgrade animal facilities at academic medical centers and research institutions, this program deserves increased funding to assist institutions in providing the facilities essential to maintain the high quality of research involving animals.

[†] Financing and Managing University Research Equipment; Association of American Universities, National Association of State Universities and Land-Grant Colleges, and Council on Government Relations, Washington, D.C.; 1985.

> *Creative federal grants programs to provide the shared research resources vital to realizing the full research potential of our nation's academic medical centers and universities should be continued and enhanced.*

Flexible funds available for deployment at the discretion of individual institutions are awarded through the NIH program of Biomedical Research Support Grants. These funds are variously used for start-up and transition support for investigators, urgently needed equipment and other resources. They are carefully husbanded to meet the unique and changing needs of each institution and to maximize its ability to sustain the extramural federal research program.

> *Maximal research productivity and optimal institutional support for the federal research program are enhanced by the provision of some flexible research funds for deployment at the discretion of the institution. Programs such as the NIH Biomedical Research Support Grants should be continued.*

Indirect Costs

There is no area of federal support for biomedical research that is more contentious than the reimbursements paid to universities for the costs they incur at a central or institutional level in support of federally funded research conducted at their facilities. The total cost of research at an institution can be divided into two categories — direct and indirect — depending on whether or not the costs can be attributed to individual research projects. Indirect costs are legitimate research expenses, documented by agreed upon accounting conventions and subject to audit. Their method of payment through a calculated average percentage of the direct costs across the entire university, however, creates a dissociation between these two equally real cost components of research and imparts an artificial quality to the indirect cost calculations. These indirect cost reimbursement policies evolved because it was not possible to assign all of their components to individual grants; yet, it is this lack of a concrete association between the direct project costs and these supporting costs at the level of the individual grants that has engendered distrust and strained relations between individual faculty researchers and administrators. In biomedical research, this distrust is further fueled by a steady shift in the proportion of total research costs expended in the direct and indirect cost categories. Despite a number of policy reviews and examinations of this issue by universities and the federal government, the legitimacy of costs in the indirect category continues to be questioned.

> *Appropriately audited research costs assigned by convention or choice to the indirect costs category are a legitimate component of the total costs of research. Payment of these costs is as critical to extramural research productivity as payment of direct costs.*

The division within the research community on this issue does not encourage thoughtful policy deliberation and invites outside intervention by budget cutters who seek to "control" research costs and decrease the federal investment rather than to optimize the productive allocation of research funds.

> *All segments of the research community should join together in a concerted effort to agree on the components and accounting of indirect costs so that these are better understood and accepted. All must agree that these are necessary costs of research for them to enjoy the confidence of the entire research community.*

As the scale and complexity of the nation's biomedical research effort have increased, it has become increasingly cumbersome to administer. Numerous, individually well-intentioned procedures, directives, guidelines, regulations, and laws have been promulgated concerning the administrative and fiscal procedures that awardee institutions must follow to be eligible for and provide accountability for federal biomedical research funds. Little attention has been paid at the federal level to the degree to which this gradual bureaucratic accretion contains redundant, contradictory, counterproductive, or simply not cost effective requirements.

The cost to the institution of meeting these requirements reduces the total dollars available to fund the research itself. Ways must be found to achieve a level of accountability that is reasonable and agreeable to both the government and the research institutions, but which is cost efficient and does away with excessive documentation. Recent efforts by the NIH to increase the jurisdiction of the institutional prior approval system for grant rebudgeting and by the White House Science Council to recommend that investigators be permitted to use up to 10 percent of their grant support on a discretionary basis for research and educational purposes and to carry forward unexpended funds from one fiscal year to the next are examples of laudable trends.

> *Concerted efforts should be made to streamline and reduce federal bureaucratic requirements that add unnecessary administrative burdens to research institutions and divert scarce research funds.*

Facilities

Recent attention in the extramural research community has focused on the declining state of science facilities in all disciplines as a growing threat to the nation's research capabilities. The absence of significant federal investment in extramural facilities through competitive construction grants programs for over a decade is cited as a prime reason for this decline. This lack of support for facilities also is blamed for the growing trend toward individual universities seeking direct congressional appropriations for science buildings.

The inevitable deterioration of facilities built before 1970 and the limited resources to keep pace with the growth in scale and complexity of the research effort have taken their toll. However, at least in biomedical research, a thorough study of the nature and degree of these deficiencies in facilities has not been undertaken and is urgently needed to guide responsible policy decisions and program planning. Especially in the area of physical plant and fixed equipment, the needs of different disciplines are bound to vary, and decisions concerning the types of facilities and the means through which they should be funded should be field specific.

> *The federal government should assume responsibility for specific and ongoing studies to ascertain the state of the physical plant in the nation's universities and academic medical centers. Such studies are the necessary basis for policy decisions and program planning to assure that the capacity of the national effort in biomedical research is sustained.*

Based on results of such studies, policies should be developed to determine the yearly scale of the federal investment in maintaining and rejuvenating facilities for federally funded biomedical research. The methods by which these capital costs are met also should be carefully considered. Until 1969 the NIH had a Health Research Facilities Grants Program through which yearly appropriations for major construction and renovation projects were channeled. The lapsing of authority for this program has undoubtedly contributed to the lack of major resources to revitalize the physical plant in the biomedical sciences. A direct facilities grants program would have the advantages that applications would be competitive and their relative scientific merit could be weighed. Funds would be provided to NIH and ADAMHA specifically for buildings in the fields of biomedical and behavioral sciences. The scale of the federal investment in capital costs for buildings would be reviewed yearly in competition with the federal appropriations for other research programs and based on a clear policy decision about resource allocation.

While an authorized program would permit capital costs to be provided through direct federal grant construction support, recovery of private capital investments is currently possible through federal reimbursement of use/depreciation charges and through indirect cost recovery of interest paid on buildings constructed through privately incurred debt. In 1985, NIH invested $13.1 million in extramural research facilities through several specific categorical construction authorities and $70 million through use allowance and depreciation costs. These reimbursement methods by which federal funds can be tapped to contribute to the financing of facilities at research institutions provide an important degree of flexibility for universities. They have the added virtue that they provide funding through mechanisms that intimately link federal funds for facilities with the continued ability of that university or academic medical center to be the venue for a large volume of merit-reviewed, competitive research grant funding. They have the disadvantage that federal investment in facilities is not subject to review of the scale of investment through the appropriations process, where it is weighed in competition with funding for other research programs when scarce funds are allocated, and that funds to pay for buildings in a given field of science through indirect cost reimbursement are partially provided from the budgets of agencies in other fields of science.

> *Federal policy should be developed to determine how documented need for research facilities should be met under conditions of fiscal constraint on research allocations. Programs of direct merit reviewed capital grants and opportunities for phased recovery of capital investments from non-federal sources should be provided. The scale of the federal investment from all sources should be monitored and weighed with other investment priorities.*

IV. FORMULATION OF SCIENCE POLICY

Over the past 40 years, a complex system for federal policy-making in the biomedical and behavioral sciences has evolved. In theory, there are interrelated but separate roles assigned to each of the major participants; the Congress sets overall goals and allocates resources within very generic categories, and the executive branch, through its departments and agencies, establishes working priorities and determines the actual means to achieve these goals. In practice, the system is highly pluralistic. As the size and complexity of the federal biomedical research enterprise has grown, and as its successes and potential have become better known to the public, the number and variety of groups and persons seeking to influence federal health research policy has grown commensurately.

The formulation of federal biomedical research policy, because it involves the expenditure of public funds, rests with the President and the Congress. As fiscal constraints have become more dominant, resource allocation has become a major arena in which conflicts related to policy priorities are expressed. As a result, both the White House Office of Management and Budget (OMB) and the congressional appropriations committees have become major foci for research policy and priority decisions. Recent policy emanating from the OMB has caused particular concern because of the apparent priority given to the current fiscal exigencies over scientific considerations.

The priority of investment in science *vis a vis* other federal endeavors and the relative priority accorded different fields of science in the allocation of limited federal resources are rightly public decisions. Within any field of science, such as the biomedical and behavioral sciences basic to medicine, subsidiary goals must be chosen and priorities established to achieve the generic goal of advancing biologic knowledge and improving human health. While all segments of society should have a voice in setting overarching federal priorities and scientists should participate both as citizens and experts in these debates, it is increasingly critical that the best scientific advice be available to Congress and the executive branch as specific goals and priorities are established within a given scientific domain. Indeed, as the formulation of policy and decision-making about the allocation of resources move from general to more specific questions about the means to achieve a given goal, there must be a corresponding shift from the public and political arena to the professional administrators of the federal biomedical research enterprise working in concert with the scientists themselves.

The present system for obtaining advice about the allocation of resources within the domain of biomedical and behavioral research is pluralistic and decentralized. This has the advantage that all shades of opinion are represented through both formal and informal channels, that laymen as well as scientists present their views, and that no aspect of the enterprise lacks adherents and advocates. It has the disadvantage that this chorus of opinion is cacophonous and often contradictory. The scientific community is concerned to ensure that Congress and the President receive impartial, realistic, and timely advice from scientists concerning goals, priorities, and means to achieve goals in the field of biomedical research so that federal decision-making may be as informed and effective as possible.

Formal mechanisms to achieve the best consensus of the scientific community on key policy issues and priorities for biomedical research would be a useful adjunct to the present process. Such mechanisms would focus debate and provide a forum for resolution to the extent that they were able to pursue practical policy questions in a realistic time frame as well as advise on long-range priority setting. While they would address issues of public concern, they would not be mechanisms for achieving agreement between scientists and the public but for presenting scientific advice. Potential forums for providing such scientific advice to the President and Congress currently exist in the institute advisory councils of the NIH and ADAMHA and the National Academy of Sciences/Institute of Medicine. To fulfill this role, these bodies must be charged with providing such consensus advice in a fashion more timely and germane to public policy debates than they provide in their current roles.

ADVICE TO THE EXECUTIVE BRANCH

The advisory councils of the individual institutes of the NIH and ADAMHA are duly constituted bodies chartered to provide policy advice and establish priorities within categorical disciplines as well as approve funding allocations within their respective institutes. These councils are charged to debate and develop recommendations on policies and priorities on broader issues germane to biomedical and behavioral research. Some of this is done in conjunction with the individual institute 5 year plans. To provide the consensus and broad view most useful to the public debate, it is important that the deliberations of the councils be sent directly to the Director of NIH or Administrator of ADAMHA to be integrated with the views of other councils and the senior agency staff so that the overall priorities that are recommended balance the views of differing disciplines. Such consensus should be achieved through the use of an integrating advisory mechanism that remains within the respective agency. The final recommendations of each agency should be publicly available to assist in national policy debates.

To effectively serve as a scientific advisory body, each council requires an appropriate number of scientists drawn from the top ranks of the relevant academic disciplines. Such high quality active scientists broadly representative of the national cadre of working scientists in each discipline must continually be recruited to fill the ranks of the advisory councils to ensure that the most knowledgeable advice is obtained. The scientific expertise and calibre of these critical advisory bodies is essential to their current function and would be even more essential in an expanded role as policy advisors to NIH as a whole and ultimately the executive branch and the President.

Through these duly constituted standing panels of advisors, scientific advice with a disciplinary focus could be formally developed, integrated at the agency level, and presented through the Office of the Assistant Secretary for Health, who then provides overall biomedical and behavioral research advice to the Department of Health and Human Services and eventually to the President. While this administrative hierarchy is currently in place, the key changes that would cause it to function as a more useful biomedical research policy advisory mechanism would be to shift the focus of the advisory council towards providing such advice, thus making them the fulcrum for much of the debate that now occurs in a decentralized and fragmented way, and to require the formulation of timely recommendations on key issues from each of the research agencies.

The advisory councils of the individual institutes at NIH and ADAMHA are charged to advise on research policy and priorities and should submit their recommendations to the Director of NIH or Administrator of ADAMHA. The Directors in turn should develop and present consensus scientific advice on key issues in research policy to the administration via the Office of the Assistant Secretary for Health.

The executive branch also receives independent advice on science policy from the White House Office of Science and Technology Policy. This body was established to provide the President with advice that represents and integrates the major domains of science and examines issues of government-wide research policy. For this office to function optimally in providing such advice, it is important that it include strong representation from the life sciences, including a prominent senior scientist from the biomedical and behavioral research community who can provide expert advice on biomedical research policy and see that the unique interests of the medical and life sciences are integrated into the overall science enterprise.

The President's Office of Science and Technology Policy should include strong senior representation from the fields of biomedical and behavioral sciences.

ADVICE TO CONGRESS

While Congress has access to the views of the biomedical and behavioral research agencies through both oversight hearings and mandated reports, and is also beseiged by many professional and public constituencies who speak for segments of the research community, it lacks a single formal mechanism for obtaining the highest level of advice in its efforts to formulate federal policy for support of biomedical and behavioral research. An independent advisory structure could provide an ongoing appraisal of the state of biomedical and behavioral sciences research, highlighting opportunities for current progress, areas of promise, and neglected disciplines or themes. Besides this ongoing function of evaluating the federal directions in biomedical and behavioral research, such an advisory body could provide timely counsel in formulating the health and life sciences research budgets and assist Congress in establishing short- and long-term funding priorities.

In theory, a new entity is not needed to fill this role. The National Academy of Sciences was chartered by President Lincoln in 1863 to serve as an official advisor to the federal government on any question of science or technology. It has fulfilled this role admirably in undertaking long-term studies on key policy issues and in providing a forum for debate and opportunities to seek consensus within the scientific community on many aspects of scientific policy and priority setting. These valuable functions should continue. The NAS could also organize itself through the Institute of Medicine to meet the need for timely advice and undertake the task of generating a consensus position on issues of immediate concern to Congress and the administration. Its membership of eminent scientists as well as other members of the science community could be tapped to deliberate such issues and charged to provide impartial and balanced scientific advice in areas of budget and resource allocation that is cognizant of the realistic pressures and choices faced by Congress and that presents a considered scientific judgment responsive to public aspirations and concerns.

The National Academy of Sciences through the Institute of Medicine should assume a strengthened role as an advisory body to Congress, the executive branch, and the public on issues of topical concern in the biomedical sciences and in areas where resource allocation and program priority decisions are being made under pressures of fiscal and time constraints.

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